Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptaeal1624

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * Welcome to STN International * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 3	OCT 19	BEILSTEIN updated with new compounds
NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
NEWS 7	DEC 04	LINPADOCDB now available on STN
NEWS 8	DEC 14	BEILSTEIN pricing structure to change
NEWS 9	DEC 17	USPATOLD added to additional database clusters
NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 23	FEB 08	STN Express, Version 8.3, now available
NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:38:20 ON 03 MAR 2008

=> file rg
'RG' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'HOME'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.05	1.05

FILE 'REGISTRY' ENTERED AT 15:41:17 ON 03 MAR 2008
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STRUCTURE FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10506998erich.str

Cy

1

```
chain nodes :
1  8  18  22
ring nodes :
2  3  4  5  6  7  10  11  12  13  14  15
chain bonds :
2-8
ring bonds :
2-3  2-4  3-5  4-6  5-7  6-7  10-11  10-15  11-12  12-13  13-14  14-15
exact/norm bonds :
2-3  2-4  2-8  3-5  4-6  5-7  6-7
normalized bonds :
10-11  10-15  11-12  12-13  13-14  14-15


G1:C,N

G2:H,X,OH,NH,NH2,NH3,NO2,Ak,CF3,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,C,O,
S

G3:H,OH,NH,NH2,NH3,Ak,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO,Cb

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:CLASS  10:Atom  11:Atom
12:Atom  13:Atom  14:CLASS  15:Atom  18:CLASS  19:Atom  22:CLASS  23:Atom



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
```

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 15:42:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 173569 TO ITERATE

100.0% PROCESSED 173569 ITERATIONS 64620 ANSWERS
SEARCH TIME: 00.00.03

L2 64620 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 178.36 179.41

FILE 'CAPLUS' ENTERED AT 15:42:10 ON 03 MAR 2008
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FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l2 full
L3 16610 L2

=> s l3 and inhibit!
147012 INHIBIT!
L4 466 L3 AND INHIBIT!

=> s l4 and histone deacetylase
35968 HISTONE
26886 HISTONES
41605 HISTONE
(HISTONE OR HISTONES)
8050 DEACETYLASE
1910 DEACETYLASES
8499 DEACETYLASE
(DEACETYLASE OR DEACETYLASES)
6882 HISTONE DEACETYLASE
(HISTONE(W)DEACETYLASE)
L5 2 L4 AND HISTONE DEACETYLASE

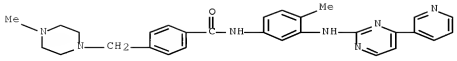
=> d ibib abs hitstr tot

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1133489 CAPLUS Full-text
DOCUMENT NUMBER: 146:155495
TITLE: Cytotoxic effects of histone deacetylase inhibitor FK228 (depsipeptide, formally named FR901228) in combination with conventional anti-leukemia/lymphoma agents against human leukemia/lymphoma cell lines
AUTHOR(S): Kano, Yasuhiko; Akutsu, Miyuki; Tsunoda, Saburo; Izumi, Tohru; Kobayashi, Hiroyuki; Mano, Hiroyuki; Furukawa, Yusuke
CORPORATE SOURCE: Division of Hematology, Tochigi Cancer Center, 4-9-13 Yonan, Utsunomiya, Japan
SOURCE: Investigational New Drugs (2006), Volume Date 2007, 25(1), 31-40
CODEN: INNDDK; ISSN: 0167-6997
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB FK228 is a novel antitumor depsipeptide that inhibits histone deacetylases and restores the expression of genes aberrantly suppressed in cancer cells. This agent was shown to have broad antitumor activity in preclin. studies, and is currently under phase I/II evaluations. Because of its wide spectrum of actions, it is reasonable to consider the combination with other anticancer drugs in clin. application. We studied the cytotoxic interaction of FK228 in combination with conventional antileukemic agents using human promyelocytic leukemia HL60, Philadelphia chromosome-pos. (Ph+) chronic myelogenous leukemia KU-812, T-cell lymphoblastic leukemia MOLT3 and Burkitt's lymphoma Raji cell lines. For the combination of FK228 and imatinib, Ph+ leukemia KU812, K562 and TCC-S cell lines were used. The cells were exposed simultaneously to FK228 and other agents for 4 days. Cell growth inhibition was determined by using 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide (MTT) assay. We used the isobologram method of Steel and Peckham to evaluate the cytotoxic interaction at the concentration of drugs that produced 80% cell growth inhibition (IC80). FK228 showed an additive effect with cytarabine, carboplatin, doxorubicin, etoposide, 4-hydroperoxy-cyclophosphamide, 6-mercaptopurine and SN-38 (active metabolite of irinotecan) in all cell lines studied. FK228 with methotrexate and vincristine showed an antagonistic effect in three and one of the four cell lines, resp. FK228 was additive with imatinib in all three Ph+ leukemia cells. Our findings suggest that FK228 is a promising candidate for combining with most anticancer agents except for methotrexate and vincristine, which produce suboptimal effects.

IT 152459-95-5, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FK228 showed additive effect in combination with anticancer drugs such as cytarabine, carboplatin, doxorubicin, etoposide, 4-hydroperoxy-cyclophosphamide, 6-mercaptopurine, SN-38 and imatinib in human leukemia/lymphoma cells)

RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (CA INDEX NAME)



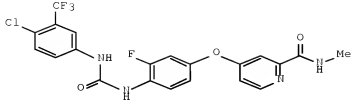
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:99470 CAPLUS Full-text
DOCUMENT NUMBER: 142:197889
TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases
INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009961	A2	20050203	WO 2004-US23500	20040722
WO 2005009961	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004259760	A1	20050203	AU 2004-259760	20040722
CA 2532865	A1	20050203	CA 2004-2532865	20040722
US 2005038080	A1	20050217	US 2004-895985	20040722
EP 1663978	A2	20060607	EP 2004-786091	20040722
EP 1663978	B1	20071128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004012219	A	20060822	BR 2004-12219	20040722
CN 1856469	A	20061101	CN 2004-80021091	20040722
JP 2006528196	T	20061214	JP 2006-521221	20040722
MX 2006PA00860	A	20060720	MX 2006-PA860	20060123
IN 2006DN00402	A	20070824	IN 2006-DN402	20060123
NO 2006000870	A	20060407	NO 2006-870	20060222

PRIORITY APPLN. INFO.:	US 2003-489102P	P	20030723
	US 2004-540326P	P	20040202
	WO 2004-US23500	W	20040722

OTHER SOURCE(S): CASREACT 142:197889
GI



I

AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

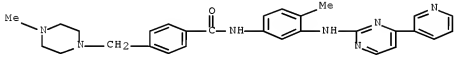
IT 220127-57-1, STI-571
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

```
=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    19.18     198.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -1.60      -1.60

FILE 'REGISTRY' ENTERED AT 15:44:41 ON 03 MAR 2008
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STRUCTURE FILE UPDATES:    2 MAR 2008  HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES:   2 MAR 2008  HIGHEST RN 1006303-40-7

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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.30     200.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -1.60

FILE 'REGISTRY' ENTERED AT 15:47:34 ON 03 MAR 2008
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STRUCTURE FILE UPDATES:    2 MAR 2008  HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES:   2 MAR 2008  HIGHEST RN 1006303-40-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

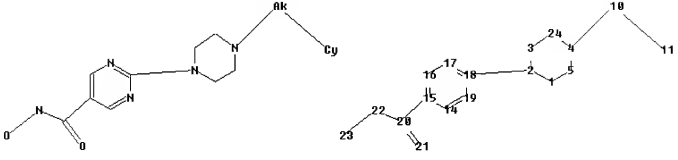
  Please note that search-term pricing does apply when
```

conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10506998allow.str



chain nodes :
10 11 20 21 22 23
ring nodes :
1 2 3 4 5 14 15 16 17 18 19 24
chain bonds :
2-18 4-10 10-11 15-20 20-21 20-22 22-23
ring bonds :
1-2 1-5 2-3 3-24 4-5 4-24 14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-2 1-5 2-3 2-18 3-24 4-10 4-5 4-24 10-11 20-21 20-22 22-23
exact bonds :
15-20
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

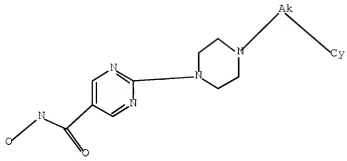
G4

G5:C,N,Zn,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 10:CLASS 11:Atom 14:Atom 15:Atom 16:Atom
17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:Atom

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR



G1 C,N
G2 Ak,NH2,NO2
G3 O
G4
G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=> s l6 full
FULL SEARCH INITIATED 15:47:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1429 TO ITERATE

100.0% PROCESSED 1429 ITERATIONS 112 ANSWERS
SEARCH TIME: 00.00.01

L7 112 SEA SSS FUL L6

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.36	379.25
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.60

FILE 'CAPLUS' ENTERED AT 15:47:58 ON 03 MAR 2008
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FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

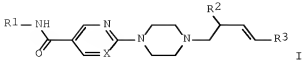
=> s l7 full
L8 9 L7

=> d ibib abs hitstr tot

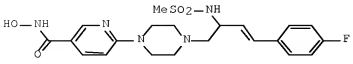
L8 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816930 CAPLUS Full-text
DOCUMENT NUMBER: 147:211903
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Marconnet-Decrane, Laurence Francoise Bernadette; Gaurrand, Sandrine Francoise Dominique; Angibaud, Patrick Rene
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082874	A1	20070726	WO 2007-EP50371	20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2006-100570 A 20060119
OTHER SOURCE(S): MARPAT 147:211903
GI



I



II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; X = N or CH; R2 = amino, alkylamino, alkoxyl, OH, etc.; R3 = (un)substituted Ph, naphthalene, or heterocycle] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 5.3, resp. Formulations containing I as active ingredients were also reported.

IT 944738-91-4P 944738-94-7P 944738-97-0P
944739-00-8P 944739-08-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

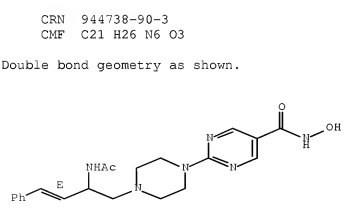
RN 944738-91-4 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-90-3
CMF C21 H26 N6 O3

Double bond geometry as shown.



CM 2

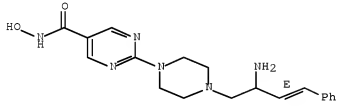
CRN 76-05-1
CMF C2 H F3 O2

RN 944738-94-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-93-6
CMF C19 H24 N6 O2

Double bond geometry as shown.



CM 2

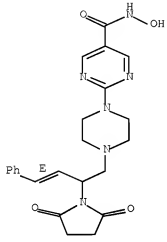
CRN 76-05-1
CMF C2 H F3 O2

RN 944738-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-96-9
CMF C23 H26 N6 O4

Double bond geometry as shown.



CM 2

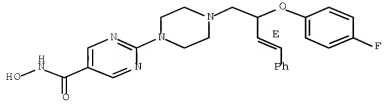
CRN 76-05-1
CMF C2 H F3 O2

RN 944739-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-99-2
CMF C25 H26 F N5 O3

Double bond geometry as shown.



CM 2

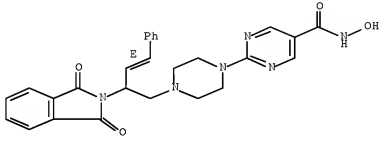
CRN 76-05-1
CMF C2 H F3 O2

RN 944739-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944739-07-5
CMF C27 H26 N6 O4

Double bond geometry as shown.



CM 2

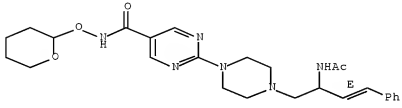
CRN 76-05-1
CMF C2 H F3 O2

IT 944739-19-9P 944739-25-7P 944739-27-9P
944739-36-0P 944739-42-8P 944739-65-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidine derivs. as histone deacetylase inhibitors)

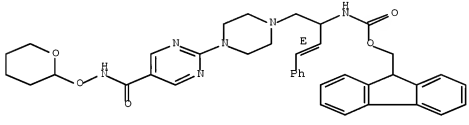
RN 944739-19-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



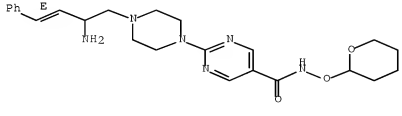
RN 944739-25-7 CAPLUS
CN Carbamic acid, N-[(2E)-3-phenyl-1-[[4-[5-[[[(tetrahydro-2H-pyran-2-yl)oxy]amino]carbonyl]-2-pyrimidinyl]-1-piperazinyl]methyl]-2-propen-1-yl]-, 9H-fluoren-9-ylmethyl ester (CA INDEX NAME)

Double bond geometry as shown.



RN 944739-27-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.

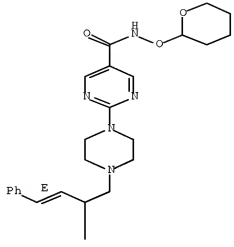


RN 944739-36-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-

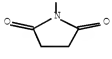
3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

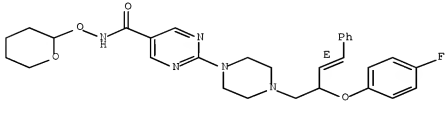


PAGE 2-A



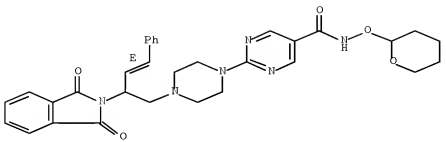
RN 944739-42-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



RN 944739-65-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

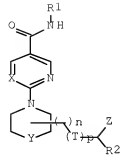
L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816806 CAPLUS Full-text
DOCUMENT NUMBER: 147:211902
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Angibaud, Patrick Rene; Van Brandt, Sven Franciscus Anna; Marconnet-Decrane, Laurence Francoise Bernadette; Roux, Bruno
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082880	A1	20070726	WO 2007-EP50379	20070116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-100571 A 20060119
OTHER SOURCE(S): MARPAT 147:211902
GI



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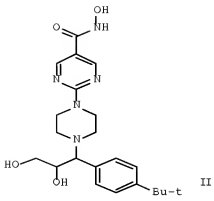


II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; R2 = -CH2OH, -CH2OCH3, -CH2OCH2CH3, or -CH2CH(OH)CH2OH; T = N(R3), where R3 = H, alkyl, cycloalkyl, etc.; X = N or CH; Y = O, NH, CH2, etc.; n = 0-1; p = 0-1, provided that when p = 0 then n = 0 and Y = N, and -CH(R2)-Z is attached to Y; Z = (un)substituted aryl or heteroaryl] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 7.1, resp. Formulations containing I as active ingredients were also reported.

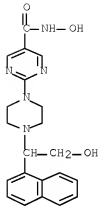
IT 944712-03-2P 944712-05-4P 944712-07-6P
944712-09-8P 944712-10-1P 944712-12-3P
944712-14-5P 944712-16-7P 944712-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944712-03-2 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-02-1
CMF C21 H23 N5 O3



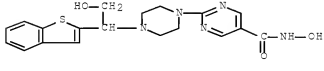
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-05-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-04-3
CMF C19 H21 N5 O3 S



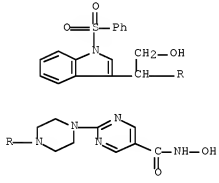
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-07-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

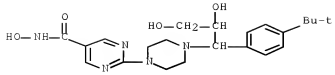
CRN 944712-06-5
CMF C25 H26 N6 O5 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

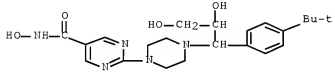
RN 944712-09-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 944712-10-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 944712-09-8
CMF C22 H31 N5 O4



CM 2

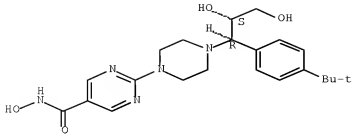
CRN 76-05-1
CMF C2 H F3 O2

RN 944712-12-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-11-2
CMF C22 H31 N5 O4

Absolute stereochemistry.



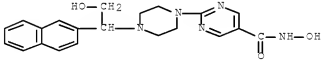
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-14-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 944712-13-4
CMF C21 H23 N5 O3



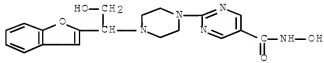
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-16-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(2-benzofuranyl)-2-hydroxyethyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-15-6
CMF C19 H21 N5 O4



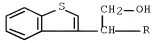
CM 2

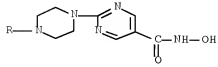
CRN 76-05-1
CMF C2 H F3 O2

RN 944712-18-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-3-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-17-8
CMF C19 H21 N5 O3 S



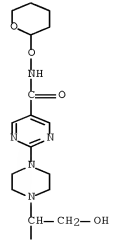


CM 2

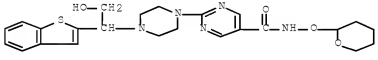
CRN 76-05-1
CMF C2 H F3 O2

IT 944712-19-0P 944712-20-3P 944712-23-6P
944712-27-0P 944712-30-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidine derivs. as histone deacetylase inhibitors)
RN 944712-19-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

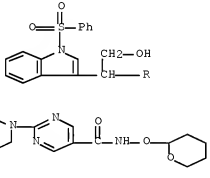
PAGE 1-A



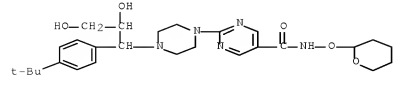
RN 944712-20-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 944712-23-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

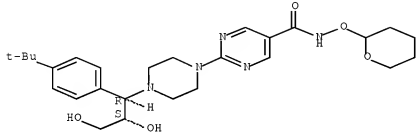


RN 944712-27-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 944712-30-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

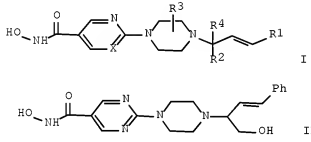
L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101446 CAPLUS Full-text
DOCUMENT NUMBER: 144:192266
TITLE: Preparation of substituted propenyl piperazine derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Brandt, Sven Franciscus Anna; Van Emelen, Kristof; Angibaud, Patrick Rene; Marconnet-Decrane, Laurence Francoise Bernadette; Arts, Janine
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010749	A2	20060202	WO 2005-EP53611	20050725
WO 2006010749	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005266311	A1	20060202	AU 2005-266311	20050725

CA 2572971	A1	20060202	CA 2005-2572971		20050725
EP 1776358	A2	20070425	EP 2005-777776		20050725
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
CN 1993356	A	20070704	CN 2005-80025487		20050725
KR 2007043978	A	20070426	KR 2007-701641		20070123
US 2007135424	A1	20070614	US 2007-626215		20070123
IN 2007DN00658	A	20070803	IN 2007-DN658		20070124
MX 2007001119	A	20070315	MX 2007-1119		20070126
NO 2007001117	A	20070227	NO 2007-1117		20070227
PRIORITY APPLN. INFO.:			EP 2004-77171	A	20040728
			US 2004-592357P	P	20040729
			WO 2005-EP53611	W	20050725

OTHER SOURCE(S): CASREACT 144:192266; MARPAT 144:192266

GI



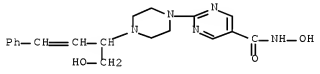
I

II

AB Substituted propenyl piperazine derivs. I, wherein X is independently N or CH; R1 is Ph, naphthalenyl or heterocyclyl; wherein each of said Ph or naphthalenyl is optionally substituted with one or two substituents each independently selected from halo, alkyl, alkyloxy, poly-halo-alkyl, aryl, hydroxy, cyano, amino, alkylcarbonylamino, alkylsulfonylamino, hydroxycarbonyl, alkyloxycarbonyl, hydroxyalkyl, alkyloxymethyl, aminomethyl, alkylaminomethyl, alkylcarbonylaminomethyl, alkylsulfonylaminomethyl, aminosulfonyl, alkylaminosulfonyl or heterocyclyl; R2 is hydrogen, -CH2R5, trifluoromethyl, -C(O)-R6, or -CH-NR7R8; wherein each R5 is independently hydrogen, hydroxy, alkyloxy, alkyloxyalkyloxy, alkylcarbonyloxy, piperazinyl, N-methylpiperazinyl, morpholinyl, thiomorpholinyl, imidazolyl or triazolyl; each R6 is independently hydroxy, alkyloxy, amino or mono- or di(alkyl)amino, cycloalkylamino, hydroxyalkylamino, piperazinyl, N-methylpiperazinyl, morpholinyl or thiomorpholinyl; each R7 and R8 are independently hydrogen, alkyl, alkylcarbonyl, alkylsulfonyl, or mono- or di(alkyl)aminosulfonyl; R3 is hydrogen, hydroxymethyl, aminomethyl or mono- or di(alkyl)aminomethyl; R4 is hydrogen or alkyl; were prepared and having histone deacetylase inhibiting enzymic activity and to inhibit proliferative conditions, such as cancer and psoriasis. Thus, propenyl piperazine derivative II was prepared and tested in vitro and in nude mice as inhibitor of histone deacetylase and was better than R306465 after oral administration. P21 enzyme linked immunosorbent assay has been applied to determine the p21 protein expression level in human A2780 ovarian carcinoma cells. In vitro assay for inhibition of histone deacetylase is reported. P21 induction was measured as the consequence of DNA damage or as the consequence of histone deacetylase inhibition. Antiproliferative activity of title compds. was determined on A2780 cells (neg. log value of the IC50, pIC50 = 7.9-8.2).

IT 875138-85-5P 875138-87-7P 875138-88-8P
875138-89-9P 875138-90-2P 875138-91-3P
875138-93-5P 875138-94-6P 875138-98-0P
875139-00-7P 875139-02-9P 875139-04-1P
875139-06-3P 875139-07-4P 875139-09-6P
875139-11-0P 875139-13-2P 875139-14-3P
875139-15-4P 875139-17-6P 875139-19-8P
875139-20-1P 875139-21-2P 875139-23-4P
875139-24-5P 875139-25-6P 875139-26-7P
875139-27-8P 875139-28-9P 875139-29-0P
875139-30-3P 875139-31-4P 875139-69-8P
875139-70-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

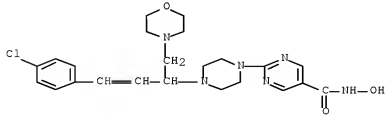
RN 875138-85-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875138-87-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-86-6
CMF C23 H29 Cl N6 O3

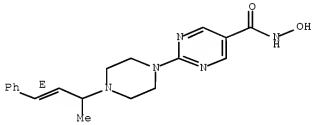


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875138-88-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

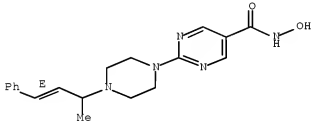


RN 875138-89-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-88-8
CMF C19 H23 N5 O2

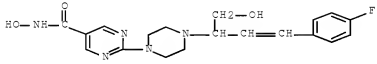
Double bond geometry as shown.



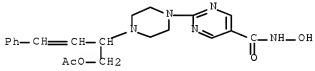
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875138-90-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



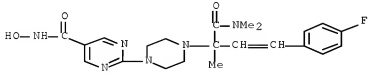
RN 875138-91-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875138-93-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-92-4
CMF C22 H27 F N6 O3

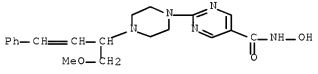


CM 2

CRN 76-05-1

CMF C2 H F3 O2

RN 875138-94-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(methoxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

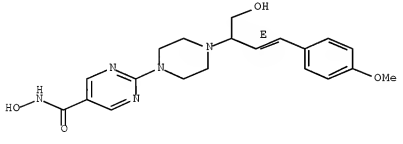


RN 875138-98-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methoxyphenyl)-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-97-9
CMF C20 H25 N5 O4

Double bond geometry as shown.



CM 2

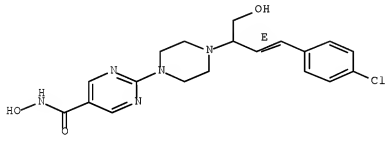
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-00-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-chlorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-99-1
CMF C19 H22 Cl N5 O3

Double bond geometry as shown.



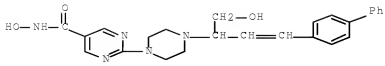
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-02-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-[1,1'-biphenyl]-4-yl-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-01-8
CMF C25 H27 N5 O3



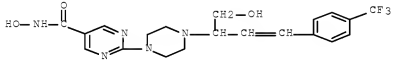
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-04-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-[4-(trifluoromethyl)phenyl]-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-03-0
CMF C20 H22 F3 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

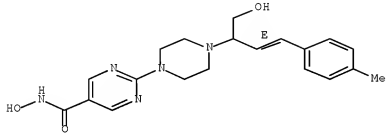
RN 875139-06-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-

methylphenyl)-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-05-2
CMF C20 H25 N5 O3

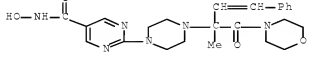
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

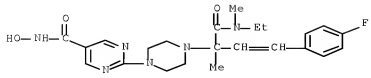
RN 875139-07-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-methyl-1-(4-morpholinylcarbonyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-09-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(ethylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-08-5
CMF C23 H29 F N6 O3



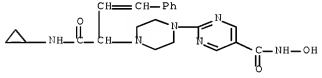
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-11-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(cyclopropylamino)carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-10-9
CMF C22 H26 N6 O3



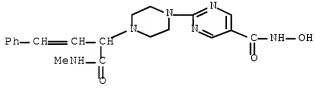
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-13-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[(methylamino)carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

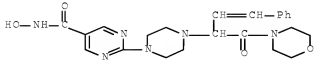
CRN 875139-12-1
CMF C20 H24 N6 O3



CM 2

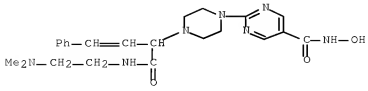
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-14-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylcarbonyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-15-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-

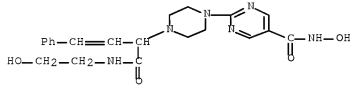
3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-17-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[[(2-hydroxyethyl)amino]carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-16-5
CMF C21 H26 N6 O4



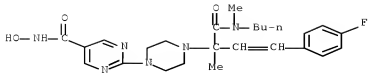
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-19-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(butylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

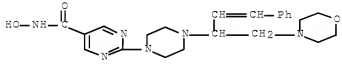
CRN 875139-18-7
CMF C25 H33 F N6 O3



CM 2

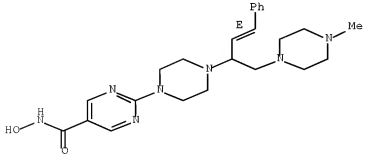
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-20-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylmethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-21-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-[(4-methyl-1-piperazinyl)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

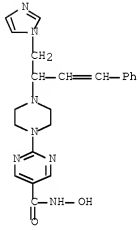
Double bond geometry as shown.



RN 875139-23-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(1H-imidazol-1-ylmethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

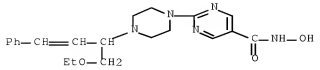
CRN 875139-22-3
CMF C22 H25 N7 O2



CM 2

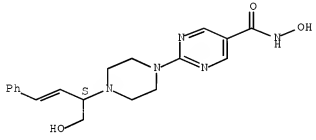
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-24-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(ethoxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



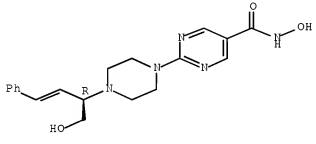
RN 875139-25-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1S)-1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



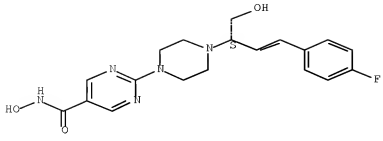
RN 875139-26-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1R)-1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

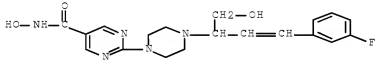


RN 875139-27-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

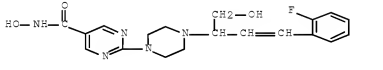
Absolute stereochemistry.
Double bond geometry unknown.



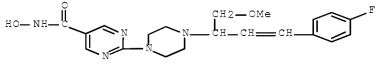
RN 875139-28-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(3-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-29-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(2-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



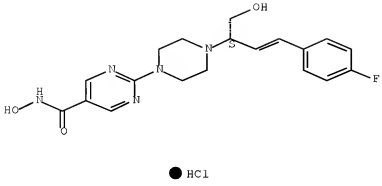
RN 875139-30-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(methoxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-31-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

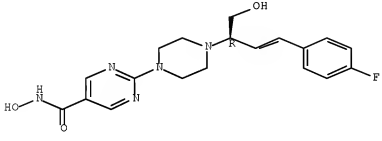
Absolute stereochemistry.

Double bond geometry unknown.



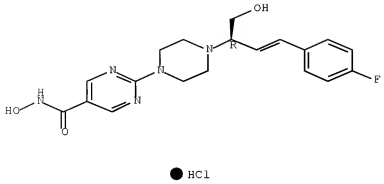
RN 875139-69-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 875139-70-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

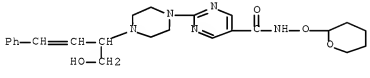
Absolute stereochemistry.
Double bond geometry unknown.



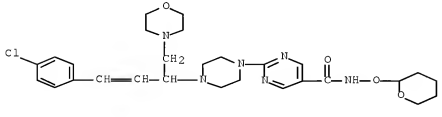
● HCl

IT 875138-54-8P 875138-59-3P 875138-62-8P
875138-66-2P 875138-70-8P 875138-73-1P
875138-77-5P 875138-78-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

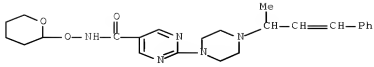
RN 875138-54-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 875138-59-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

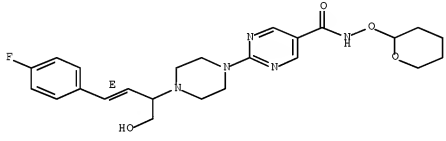


RN 875138-62-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-methyl-3-phenyl-2-propenyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

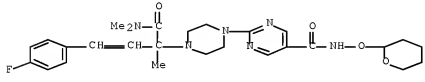


RN 875138-66-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

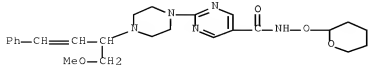
Double bond geometry as shown.



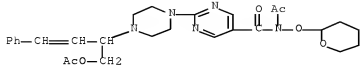
RN 875138-70-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 875138-73-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(methoxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 875138-77-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-acetyl-2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 875138-78-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-acetyl-2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

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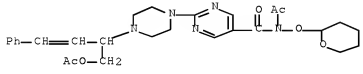
CRN 875138-77-5
CMF C28 H35 N5 O6



CM 2

CRN 144-62-7
CMF C2 H2 O4

L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300395 CAPLUS Full-text
DOCUMENT NUMBER: 142:355054
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.

SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030705	A1	20050407	WO 2004-US31591	20040924
WO 2005030705	A9	20060420		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004276337	A1	20050407	AU 2004-276337	20040924
CA 2539117	A1	20050407	CA 2004-2539117	20040924
EP 1663953	A1	20060607	EP 2004-789074	20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1882529	A	20061220	CN 2004-80034571	20040924
JP 2007506785	T	20070322	JP 2006-528279	20040924

PRIORITY APPLN. INFO.:
US 2003-505884P P 20030924
US 2003-532973P P 20031229
US 2004-561082P P 20040409
WO 2004-US31591 W 20040924

OTHER SOURCE(S): CASREACT 142:355054; MARPAT 142:355054

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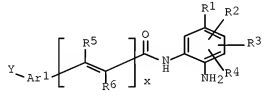

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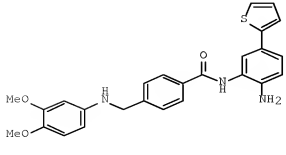
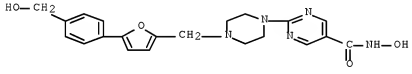


II

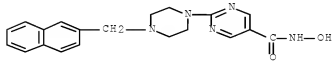
AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)- methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5- diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
603992-24-1P 603992-25-2P 603992-26-3P
603992-27-4P 603992-28-5P 604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

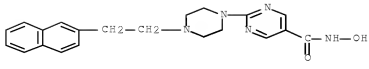
RN 603985-86-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603985-90-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-94-0 CAPLUS
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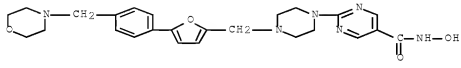
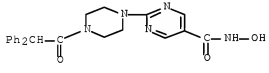
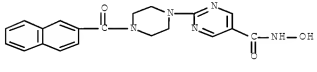


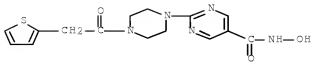
RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603992-24-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-thienylacetyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 603992-25-2 CAPLUS
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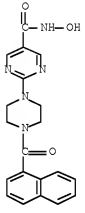
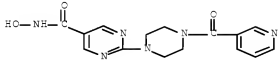
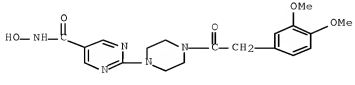


RN 603992-26-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)

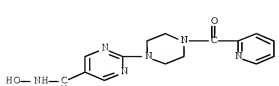


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

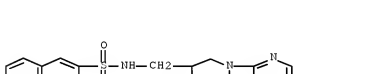


RN 603992-28-5 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 604784-81-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300394 CAPLUS Full-text
DOCUMENT NUMBER: 142:373563
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030704	A1	20050407	WO 2004-US31590	20040924

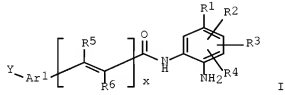
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-505884P P 20030924
US 2003-532973P P 20031229
US 2004-561082P P 20040409

OTHER SOURCE(S): MARPAT 142:373563

GI



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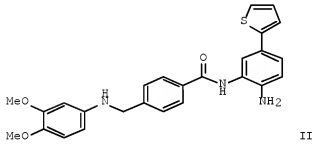


II

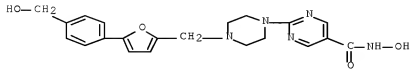
AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)- methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5- diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
603992-24-1P 603992-25-2P 603992-26-3P
603992-27-4P 603992-28-5P 694784-81-8P

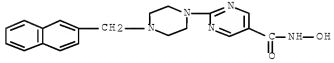
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-86-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603985-90-6 CAPLUS
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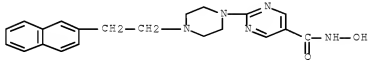
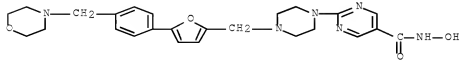


RN 603985-94-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603991-95-3 CAPLUS
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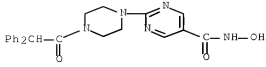
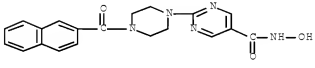


RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603992-24-1 CAPLUS
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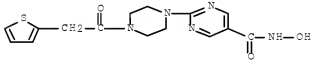

RN 603992-25-2 CAPLUS
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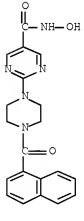
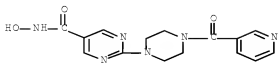
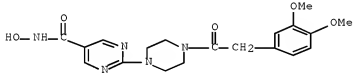


RN 603992-26-3 CAPLUS

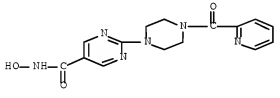
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 604784-81-8 CAPLUS
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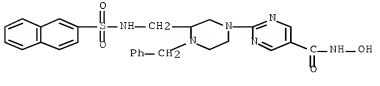

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737757 CAPLUS Full-text
DOCUMENT NUMBER: 139:276911
TITLE: Preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076438	A1	20030918	WO 2003-EP2510	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475766	A1	20030918	CA 2003-2475766	20030311
AU 2003218735	A1	20030922	AU 2003-218735	20030311
EP 1485378	A1	20041215	EP 2003-711979	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007606	A	20041221	BR 2003-7606	20030311
CN 1642948	A	20050720	CN 2003-805921	20030311
JP 2005526766	T	20050908	JP 2003-574655	20030311
NZ 534833	A	20060728	NZ 2003-534833	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02536	A	20070413	IN 2004-DN2536	20040831
US 2005165016	A1	20050728	US 2004-507084	20040908
MX 2004PA08795	A	20041126	MX 2004-PA8795	20040910
NO 2004004135	A	20040929	NO 2004-4135	20040929
PRIORITY APPLN. INFO.:			US 2002-363799P P	20020313
			WO 2002-EP14833 A	20021223
			CN 2003-805921 A3	20030311
			WO 2003-EP2510 W	20030311

OTHER SOURCE(S): MARPAT 139:276911
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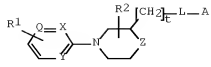

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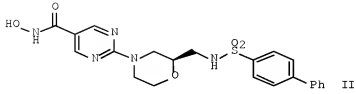


II

AB The title compds. [I; t = 0-4; Q, X, Y = N, C; Z = NH, O, CH2; R1 = CONR3R4, NHCOR7, CO(alkanediyl)SR7, etc. (wherein R3, R4 = H, OH, alkyl, etc.; R7 = H, alkyl, alkylcarbonyl, etc.); R2 = H, OH, NH2, etc.; L = NR9CO, NR9SO2, NR9CH2 (R9 = H, alkyl, cycloalkyl, etc.); A = (un)substituted Ph, cycloalkyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of (+)-II which showed pIC50 of 7.723 against HDAC, was given.

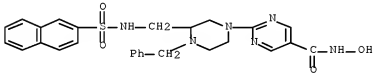
IT 604784-81-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)

RN 604784-81-8 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:737723 CAPLUS Full-text

DOCUMENT NUMBER: 139:261309

TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or diazepino)benzamides as new inhibitors of histone deacetylase

INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf

Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003218736	A1	20030922	AU 2003-218736	20030311
EP 1485353	A1	20041215	EP 2003-711980	20030311
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BR 2003008081	A	20041221	BR 2003-8081	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
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NZ 534834	A	20050729	NZ 2003-534834	20030311
JP 2005526067	T	20050902	JP 2003-574621	20030311
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US 2005107384	A1	20050519	US 2004-506998	20040908
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
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NO 2004004194	A	20041001	NO 2004-4194	20041001

PRIORITY APPLN. INFO.:

US 2002-363799P	P	20020313
WO 2002-EP14833	A	20021223
CN 2003-805921	A3	20030311
WO 2003-EP2514	W	20030311

OTHER SOURCE(S): MARPAT 139:261309

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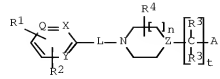

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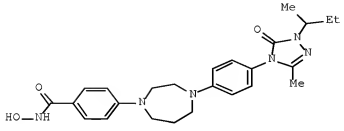

II

AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

IT 603985-87-1P 603985-89-3P 603985-91-7P
603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-87-1 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

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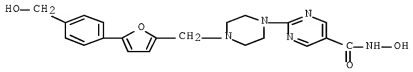
CRN 603985-86-0
CMF C21 H23 N5 O4



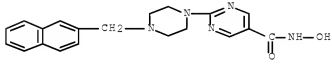
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-88-2
CMF C20 H21 N5 O2



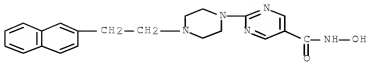
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-91-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-90-6
CMF C21 H23 N5 O2



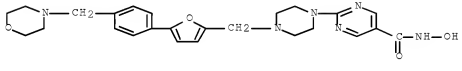
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-94-0
CMF C25 H30 N6 O4



CM 2

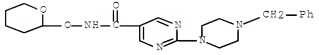
CRN 76-05-1
CMF C2 H F3 O2

IT 603986-73-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603986-73-8 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-(phenylmethyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:737586 CAPLUS Full-text

DOCUMENT NUMBER: 139:261308

TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases

INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075929	A1	20030918	WO 2003-EP2515	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476065	A1	20030918	CA 2003-2476065	20030311
AU 2003218737	A1	20030922	AU 2003-218737	20030311
EP 1485099	A1	20041215	EP 2003-711981	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007624	A	20050111	BR 2003-7624	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
JP 2005525379	T	20050825	JP 2003-574203	20030311
NZ 534832	A	20050930	NZ 2003-534832	20030311

CN 101007803	A	20070801	CN 2007-10005212		20030311
IN 2004DN02537	A	20070112	IN 2004-DN2537		20040831
ZA 2004007237	A	20050928	ZA 2004-7237		20040909
ZA 2004007235	A	20051004	ZA 2004-7235		20040909
ZA 2004007232	A	20051006	ZA 2004-7232		20040909
ZA 2004007233	A	20051006	ZA 2004-7233		20040909
ZA 2004007234	A	20051006	ZA 2004-7234		20040909
ZA 2004007236	A	20051006	ZA 2004-7236		20040909
MX 2004PA08797	A	20041126	MX 2004-PA8797		20040910
US 2005096468	A1	20050505	US 2004-507785		20040913
NO 2004004113	A	20040928	NO 2004-4113		20040928
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			WO 2002-EP14833	A	20021223
			CN 2003-805921	A3	20030311
			WO 2003-EP2515	W	20030311

OTHER SOURCE(S): MARPAT 139:261308

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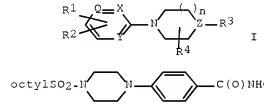


I

II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5- carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7

or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6- alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, C11-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1- 6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

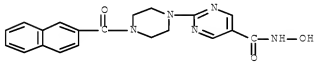
IT 603991-96-4P

RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



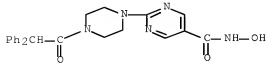
IT 603991-95-3P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P

RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

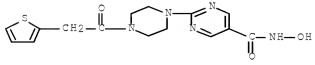
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-24-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-thienylacetyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 603992-25-2 CAPLUS
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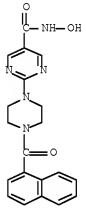

RN 603992-26-3 CAPLUS
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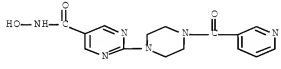
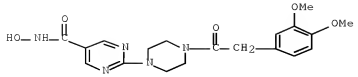


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-28-5 CAPLUS
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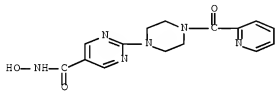
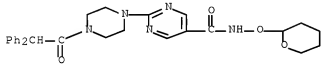


IT 603992-32-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)
RN 603992-32-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:442843 CAPLUS Full-text
DOCUMENT NUMBER: 105:42843
ORIGINAL REFERENCE NO.: 105:7101a,7104a
TITLE: Pyrimidinylpiperazines
INVENTOR(S): Kihara, Noriaki; Ishida, Tatsukazu; Isayama, Shigeru; Ishitoku, Takeshi; Tan, Hiroaki; Takahashi, Katsuya
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 28 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61043173	A	19860301	JP 1984-163771	19840806
JP 05022702	B	19930330		
PRIORITY APPLN. INFO.:			JP 1984-163771	19840806

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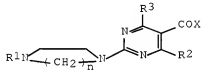

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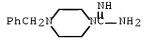


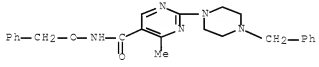
II

AB The title compds. [I, R1 = H, substituted Me, alkoxycarbonyl; R2, R3 = H, substituted alkyl; X = alkoxy, OH, (substituted) NH2; n = 2, 3], useful as herbicides against common weeds (no data), were prepared Thus, the piperazinecarboxamidine derivative II sulfate reacted with MeOCH:C(COMe)CO2Me in MeOH/aqueous NaOH at room temperature overnight to give 88% I (R1 = PhCH2, n = 2, R2 = H, R3 = Me, X = OMe).

IT 102976-25-0P 102976-32-9P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as herbicide)

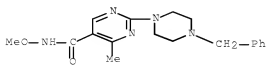
RN 102976-25-0 CAPLUS

CN 5-Pyrimidinecarboxamide, 4-methyl-N-(phenylmethoxy)-2-[4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 102976-32-9 CAPLUS

CN 5-Pyrimidinecarboxamide, N-methoxy-4-methyl-2-[4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



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DICTIONARY FILE UPDATES:   2 MAR 2008  HIGHEST RN 1006303-40-7

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http://www.cas.org/support/stngen/stndoc/properties.html

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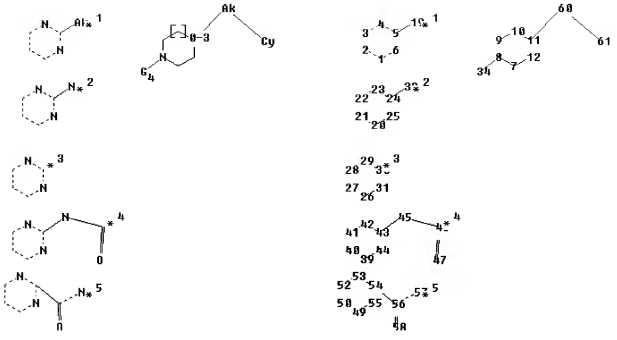

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ring nodes :
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ring bonds :
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exact/norm bonds :
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exact bonds :
54-56
isolated ring systems :
containing 1 : 7 : 20 : 26 : 39 : 49 :

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G2:Ak,NH2,NO2

G3:O

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G4:[*1],[*2],[*3],[*4],[*5]

Match level :
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L9      STRUCTURE UPLOADED

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=>
=>
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L9 HAS NO ANSWERS
L9              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


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FULL SEARCH INITIATED 17:10:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   504087 TO ITERATE

100.0% PROCESSED   504087 ITERATIONS                              8735 ANSWERS
SEARCH TIME: 00.00.07

L10        8735 SEA SSS FUL L9

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COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  236.32     669.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                    0.00      -8.80

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FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

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L11 3946 L10

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	669.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.80

FILE 'REGISTRY' ENTERED AT 17:10:46 ON 03 MAR 2008
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DICTIONARY FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7

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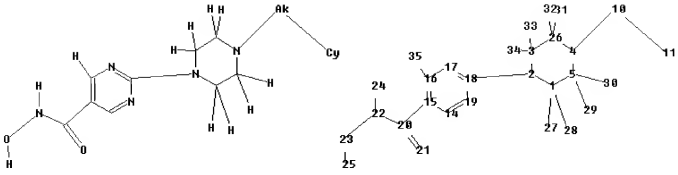
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10506998five.str



chain nodes :
10 11 20 21 22 23 24 25 27 28 29 30 31 32 33 34 35
ring nodes :
1 2 3 4 5 14 15 16 17 18 19 26
chain bonds :
1-27 1-28 2-18 3-33 3-34 4-10 5-29 5-30 10-11 15-20 16-35 20-21 20-22
22-23 22-24 23-25 26-31 26-32
ring bonds :
1-2 1-5 2-3 3-26 4-5 4-26 14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-2 1-5 2-3 2-18 3-26 4-10 4-5 4-26 10-11 20-21 20-22 22-23
exact bonds :
1-27 1-28 3-33 3-34 5-29 5-30 15-20 16-35 22-24 23-25 26-31 26-32
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

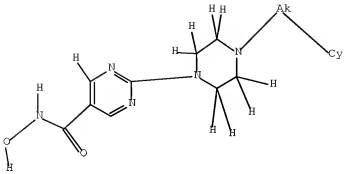
G4

G5:C,N,Zn,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 10:CLASS 11:Atom 14:Atom 15:Atom
16:Atom
17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
25:CLASS 26:Atom
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS

L12 STRUCTURE UPLOADED

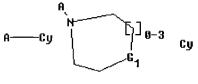
=> d l12
L12 HAS NO ANSWERS
L12 STR

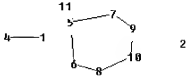


G1 C,N
G2 Ak,NH2,NO2
G3 O
G4
G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=>
Uploading C:\Program Files\Stnexp\Queries\10506998jason.str





chain nodes :
1 2 4 11
ring nodes :
5 6 7 8 9 10
chain bonds :
1-4 5-11
ring bonds :
5-6 5-7 6-8 7-9 8-10 9-10

exact/norm bonds :
1-4 5-6 5-7 5-11 6-8 7-9 8-10 9-10

G1:C,N

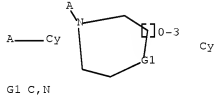
Match level :
1:Atom 2:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS

Generic attributes :
1:
Saturation   : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System   : Monocyclic

Element Count :
Node 1: Limited
    C,C3-6
    N,N0-3

L13   STRUCTURE UPLOADED

=> d l13
L13 HAS NO ANSWERS
L13   STR



G1 C,N

Structure attributes must be viewed using STN Express query preparation.

=> s l13 full
FULL SEARCH INITIATED 17:14:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 16181098 TO ITERATE

  0.9% PROCESSED   148636 ITERATIONS   36379 ANSWERS

  1.8% PROCESSED   299019 ITERATIONS   66034 ANSWERS

  2.9% PROCESSED   461612 ITERATIONS   102670 ANSWERS

  4.6% PROCESSED   740840 ITERATIONS   158301 ANSWERS

  5.0% PROCESSED   809762 ITERATIONS   172563 ANSWERS

```
  5.5% PROCESSED   890441 ITERATIONS                      190277 ANSWERS

  6.1% PROCESSED   983608 ITERATIONS                      207176 ANSWERS

  6.2% PROCESSED  1000000 ITERATIONS                      213282 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.02.03

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:     16181098 TO 16181098
PROJECTED ANSWERS:         3445667 TO  3456607

L14      213282 SEA SSS FUL L13

=>
Uploading C:\Program Files\Stnexp\Queries\10506998three.str
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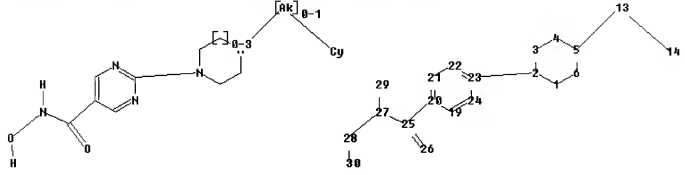



```
chain nodes :
13  14  25  26  27  28  29  30
ring nodes :
1  2  3  4  5  6  19  20  21  22  23  24
chain bonds :
2-23  5-13  13-14  20-25  25-26  25-27  27-28  27-29  28-30
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  19-20  19-24  20-21  21-22  22-23  23-24
exact/norm bonds :
1-2  1-6  2-3  2-23  3-4  4-5  5-6  5-13  13-14  25-26  25-27  27-28
exact bonds :
20-25  27-29  28-30
normalized bonds :
19-20  19-24  20-21  21-22  22-23  23-24
isolated ring systems :
containing 1 :


G1:C,N

G2:Ak,NH2,NO2

G3:O

G4

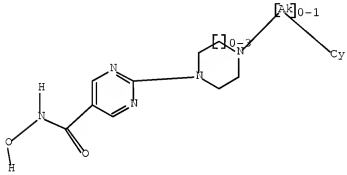
G5:C,N,Zn,H

Match level :
```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 13:CLASS 14:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS
29:CLASS 30:CLASS

L15   STRUCTURE UPLOADED

=> d l15
L15 HAS NO ANSWERS
L15   STR



G1 C,N
G2 Ak,NH2,NO2
G3 O
G4
G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=> s l15
SAMPLE SEARCH INITIATED 17:25:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   23 TO ITERATE

100.0% PROCESSED   23 ITERATIONS   11 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 173 TO   747
PROJECTED ANSWERS: 22 TO   418

L16   11 SEA SSS SAM L15

=> file caplus
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST   189.40   859.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)   SINCE FILE   TOTAL
                                                       ENTRY   SESSION

CA SUBSCRIBER PRICE 0.00 -8.80

FILE 'CAPLUS' ENTERED AT 17:25:35 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l15 full
REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 17:25:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 341 TO ITERATE

100.0% PROCESSED 341 ITERATIONS 107 ANSWERS
SEARCH TIME: 00.00.01

L17 107 SEA SSS FUL L15

L18 9 L17

=> s l18 full
L19 9 L17

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.48 1038.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE 0.00 -8.80

FILE 'CAPLUS' ENTERED AT 17:26:15 ON 03 MAR 2008

FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l19 full
L20 9 L17

=> d ibib abs hitstr tot

L20 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816930 CAPLUS Full-text
DOCUMENT NUMBER: 147:211903
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Marconnet-Decrane, Laurence Francoise Bernadette; Gaurrand, Sandrine Francoise Dominique; Angibaud, Patrick Rene
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082874	A1	20070726	WO 2007-EP50371	20070116

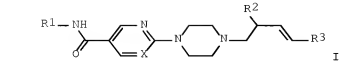
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

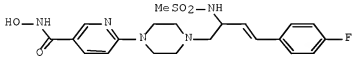
PRIORITY APPLN. INFO.: EP 2006-100570 A 20060119

OTHER SOURCE(S): MARPAT 147:211903

GI



I



II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; X = N or CH; R2 = amino, alkylamino, alkoxyl, OH, etc.; R3 = (un)substituted Ph, naphthalene, or heterocycle] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 5.3, resp. Formulations containing I as active ingredients were also reported.

IT 944738-91-4P 944738-94-7P 944738-97-0P
944739-00-8P 944739-08-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

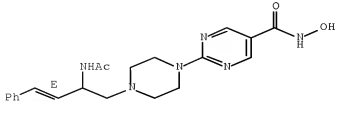
RN 944738-91-4 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-90-3
CMF C21 H26 N6 O3

Double bond geometry as shown.



CM 2

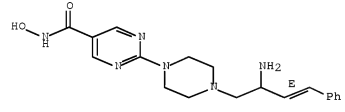
CRN 76-05-1
CMF C2 H F3 O2

RN 944738-94-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-93-6
CMF C19 H24 N6 O2

Double bond geometry as shown.



CM 2

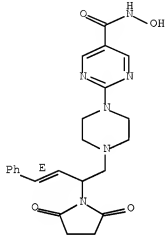
CRN 76-05-1
CMF C2 H F3 O2

RN 944738-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-96-9
CMF C23 H26 N6 O4

Double bond geometry as shown.



CM 2

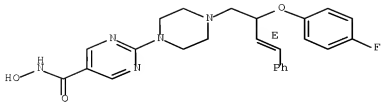
CRN 76-05-1
CMF C2 H F3 O2

RN 944739-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-99-2
CMF C25 H26 F N5 O3

Double bond geometry as shown.



CM 2

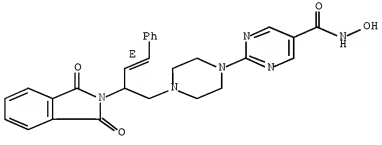
CRN 76-05-1
CMF C2 H F3 O2

RN 944739-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944739-07-5
CMF C27 H26 N6 O4

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

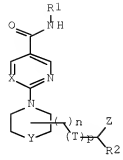
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816806 CAPLUS Full-text
DOCUMENT NUMBER: 147:211902
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Angibaud, Patrick Rene; Van Brandt, Sven Franciscus Anna; Marconnet-Decrane, Laurence Francoise Bernadette; Roux, Bruno
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

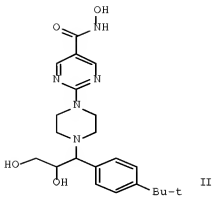
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082880	A1	20070726	WO 2007-EP50379	20070116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-100571 A 20060119
OTHER SOURCE(S): MARPAT 147:211902
GI



I



II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; R2 = -CH2OH, -CH2OCH3, -CH2OCH2CH3, or -CH2CH(OH)CH2OH; T = N(R3), where R3 = H, alkyl, cycloalkyl, etc.; X = N or CH; Y = O, NH, CH2, etc.; n = 0-1; p = 0-1, provided that when p = 0 then n = 0 and Y = N, and -CH(R2)-Z is attached to Y; Z = (un)substituted aryl or heteroaryl] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 7.1, resp. Formulations containing I as active ingredients were also reported.

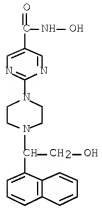
IT 944712-03-2P 944712-05-4P 944712-07-6P
944712-09-8P 944712-10-1P 944712-12-3P
944712-14-5P 944712-16-7P 944712-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944712-03-2 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-02-1
CMF C21 H23 N5 O3



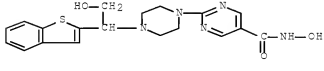
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-05-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-04-3
CMF C19 H21 N5 O3 S



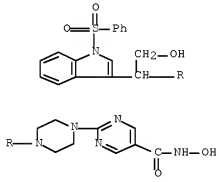
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-07-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

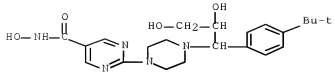
CRN 944712-06-5
CMF C25 H26 N6 O5 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

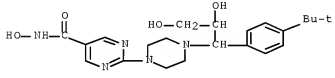
RN 944712-09-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 944712-10-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 944712-09-8
CMF C22 H31 N5 O4



CM 2

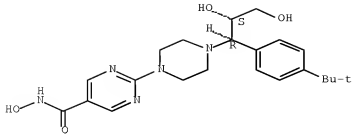
CRN 76-05-1
CMF C2 H F3 O2

RN 944712-12-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-11-2
CMF C22 H31 N5 O4

Absolute stereochemistry.



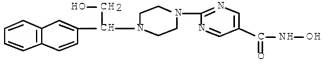
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-14-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 944712-13-4
CMF C21 H23 N5 O3



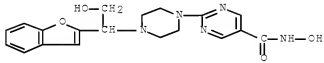
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 944712-16-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(2-benzofuranyl)-2-hydroxyethyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-15-6
CMF C19 H21 N5 O4



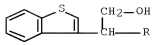
CM 2

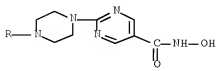
CRN 76-05-1
CMF C2 H F3 O2

RN 944712-18-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-3-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-17-8
CMF C19 H21 N5 O3 S





CM 2

CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:485854 CAPLUS Full-text
DOCUMENT NUMBER: 146:482095
TITLE: Preparation of squaric acid derivatives as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 37pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007048767	A1	20070503	WO 2006-EP67656	20061023

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2005-110080 A 20051027

OTHER SOURCE(S): MARPAT 146:482095

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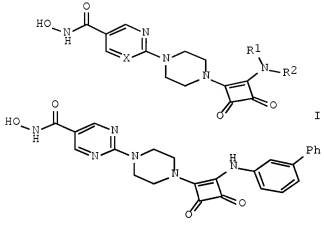
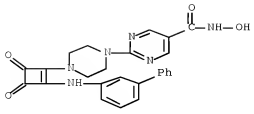


AB Title compds. I [wherein X = N or CH; R1, R2 = H, alkyl, Ph, etc.;] or N-oxides, pharmaceutically acceptable salts and stereoisomers thereof were prepared as histone deacetylase (HDAC) inhibitors. For instance, successive condensation of 3,4-diethoxy-3-cyclobutene-1,2-dione with 3-aminobiphenyl and 2-(1-piperazinyl)pyrimidine-5-carboxylic acid Et ester, ester hydrolysis, condensation of the resultant acid with NH2O-THP, and deprotection with TFA gave hydroxamic acid II. This compds. showed inhibition against HDAC with pIC50 = 7.7. The invented compds. are useful for the treatment of proliferative diseases.

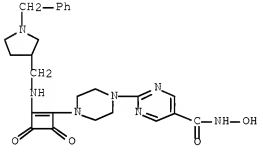
IT 935670-93-2P 935670-95-4P 935670-97-6P
935670-99-8P 935671-01-5P 935671-03-7P
935671-05-9P 935671-07-1P 935671-09-3P
935671-11-7P 935671-13-9P 935671-15-1P
935671-17-3P 935671-19-5P 935671-21-9P
935671-23-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as histone deacetylase (HDAC) inhibitors for treatment of proliferative diseases)

RN 935670-93-2 CAPLUS

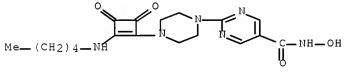
CN 5-Pyrimidinecarboxamide, 2-[4-[2-([1,1'-biphenyl]-3-ylamino)-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



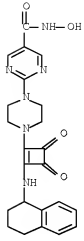
RN 935670-95-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[[1-(phenylmethyl)-3-pyrrolidinyl]methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



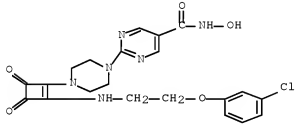
RN 935670-97-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-(pentylamino)-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



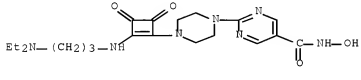
RN 935670-99-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-01-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[2-(3-chlorophenoxy)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-03-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[3-(diethylamino)propyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-05-9 CAPLUS
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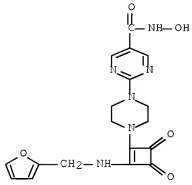
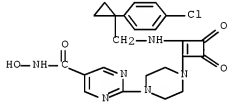
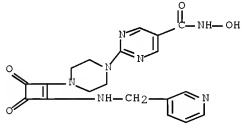


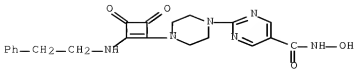
RN 935671-07-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[[1-(4-chlorophenyl)cyclopropyl]methyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



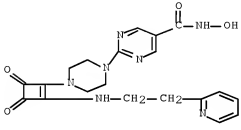
RN 935671-09-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(3-pyridinylmethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



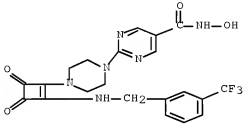
RN 935671-11-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(2-phenylethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



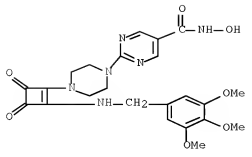
RN 935671-13-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[2-(2-pyridinyl)ethyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



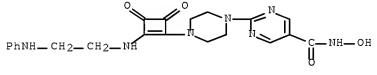
RN 935671-15-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[[3-(trifluoromethyl)phenyl]methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



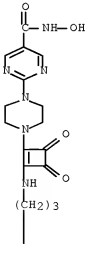
RN 935671-17-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[(3,4,5-trimethoxyphenyl)methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



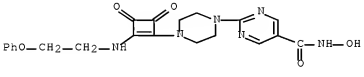
RN 935671-19-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[2-(phenylamino)ethyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-21-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-23-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(2-phenoxyethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101446 CAPLUS Full-text
DOCUMENT NUMBER: 144:192266
TITLE: Preparation of substituted propenyl piperazine derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Brandt, Sven Franciscus Anna; Van Emelen, Kristof; Angibaud, Patrick Rene; Marconnet-Decrane, Laurence Francoise Bernadette; Arts, Janine
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010749	A2	20060202	WO 2005-EP53611	20050725
WO 2006010749	A3	20060608		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005266311	A1	20060202	AU 2005-266311	20050725
CA 2572971	A1	20060202	CA 2005-2572971	20050725

EP 1776358 A2 20070425 EP 2005-777776 20050725
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CN 1993356 A 20070704 CN 2005-80025487 20050725
KR 2007043978 A 20070426 KR 2007-701641 20070123
US 2007135424 A1 20070614 US 2007-626215 20070123
IN 2007DN00658 A 20070803 IN 2007-DN658 20070124
MX 200701119 A 20070315 MX 2007-1119 20070126
NO 200700117 A 20070227 NO 2007-117 20070227
PRIORITY APPLN. INFO.: EP 2004-77171 A 20040728
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WO 2005-EP53611 W 20050725
OTHER SOURCE(S): CASREACT 144:192266; MARPAT 144:192266

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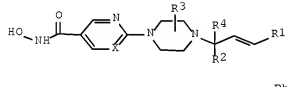

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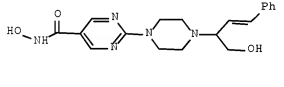


II

AB Substituted propenyl piperazine derivs. I, wherein X is independently N or CH; R1 is Ph, naphthalenyl or heterocyclyl; wherein each of said Ph or naphthalenyl is optionally substituted with one or two substituents each independently selected from halo, alkyl, alkyloxy, poly-halo-alkyl, aryl, hydroxy, cyano, amino, alkylcarbonylamino, alkylsulfonylamino, hydroxycarbonyl, alkyloxycarbonyl, hydroxyalkyl, alkyloxymethyl, aminomethyl, alkylaminomethyl, alkylcarbonylaminomethyl, alkylsulfonylaminomethyl, aminosulfonyl, alkylaminosulfonyl or heterocyclyl; R2 is hydrogen, -CH2R5, trifluoromethyl, -C(O)-R6, or -CH-NR7R8; wherein each R5 is independently hydrogen, hydroxy, alkyloxy, alkyloxyalkyloxy, alkylcarbonyloxy, piperazinyl, N-methylpiperazinyl, morpholinyl, thiomorpholinyl, imidazolyl or triazolyl; each R6 is independently hydroxy, alkyloxy, amino or mono- or di(alkyl)amino, cycloalkylamino, hydroxyalkylamino, piperazinyl, N-methylpiperazinyl, morpholinyl or thiomorpholinyl; each R7 and R8 are independently hydrogen, alkyl, alkylcarbonyl, alkylsulfonyl, or mono- or di(alkyl)aminosulfonyl; R3 is hydrogen, hydroxymethyl, aminomethyl or mono- or di(alkyl)aminomethyl; R4 is hydrogen or alkyl; were prepared and having histone deacetylase inhibiting enzymic activity and to inhibit proliferative conditions, such as cancer and psoriasis. Thus, propenyl piperazine derivative II was prepared and tested in vitro and in nude mice as inhibitor of histone deacetylase and was better than R306465 after oral administration. P21 enzyme linked immunosorbent assay has been applied to determine the p21 protein expression level in human A2780 ovarian carcinoma cells. In vitro assay for inhibition of histone deacetylase is reported. P21 induction was measured as the consequence of DNA damage or as the consequence of histone deacetylase inhibition. Antiproliferative activity of title compds. was determined on A2780 cells (neg. log value of the IC50, pIC50 = 7.9-8.2).

IT 875138-85-5P 875138-87-7P 875138-88-8P

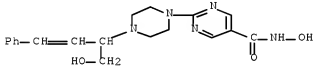
875138-89-9P 875138-90-2P 875138-91-3P
875138-93-5P 875138-94-6P 875138-98-0P
875139-00-7P 875139-02-9P 875139-04-1P
875139-06-3P 875139-07-4P 875139-09-6P
875139-11-0P 875139-13-2P 875139-14-3P
875139-15-4P 875139-17-6P 875139-19-8P
875139-20-1P 875139-21-2P 875139-23-4P
875139-24-5P 875139-25-6P 875139-26-7P
875139-27-8P 875139-28-9P 875139-29-0P
875139-30-3P 875139-31-4P 875139-69-8P
875139-70-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

RN 875138-85-5 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

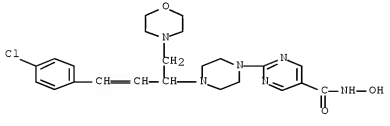


RN 875138-87-7 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-86-6
CMF C23 H29 Cl N6 O3

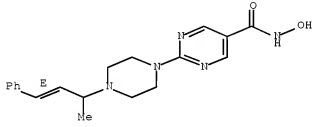


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875138-88-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

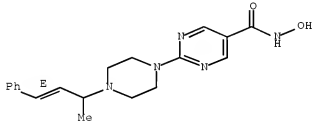


RN 875138-89-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-88-8
CMF C19 H23 N5 O2

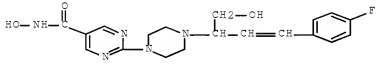
Double bond geometry as shown.



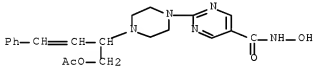
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875138-90-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



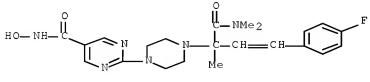
RN 875138-91-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875138-93-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-92-4
CMF C22 H27 F N6 O3

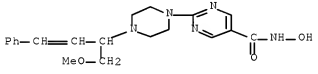


CM 2

CRN 76-05-1

CMF C2 H F3 O2

RN 875138-94-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(methoxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

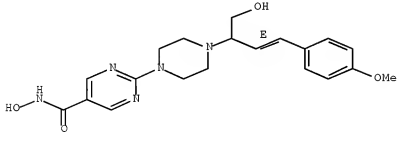


RN 875138-98-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methoxyphenyl)-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-97-9
CMF C20 H25 N5 O4

Double bond geometry as shown.



CM 2

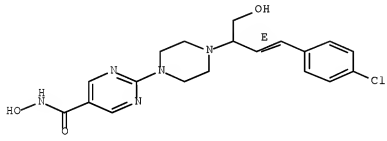
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-00-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-chlorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875138-99-1
CMF C19 H22 Cl N5 O3

Double bond geometry as shown.



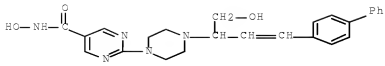
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-02-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-[1,1'-biphenyl]-4-yl-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-01-8
CMF C25 H27 N5 O3



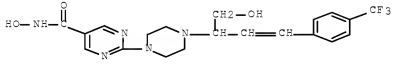
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-04-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-[4-(trifluoromethyl)phenyl]-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-03-0
CMF C20 H22 F3 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

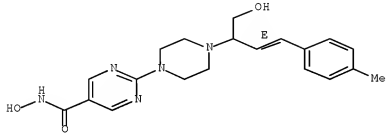
RN 875139-06-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-

methylphenyl)-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-05-2
CMF C20 H25 N5 O3

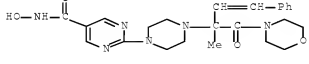
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

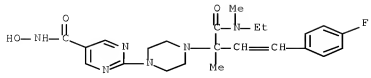
RN 875139-07-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-methyl-1-(4-morpholinylcarbonyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-09-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(ethylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-08-5
CMF C23 H29 F N6 O3



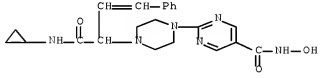
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-11-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(cyclopropylamino)carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-10-9
CMF C22 H26 N6 O3



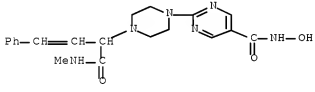
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-13-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[(methylamino)carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

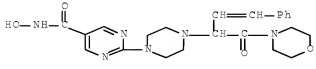
CRN 875139-12-1
CMF C20 H24 N6 O3



CM 2

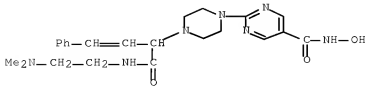
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-14-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylcarbonyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-15-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-

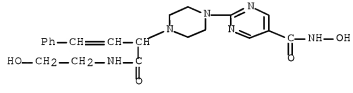
3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-17-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[[(2-hydroxyethyl)amino]carbonyl]-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 875139-16-5
CMF C21 H26 N6 O4



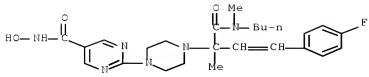
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 875139-19-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(butylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propenyl]-1-piperazinyl]-N-hydroxy-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

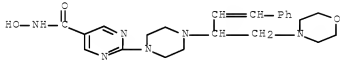
CRN 875139-18-7
CMF C25 H33 F N6 O3



CM 2

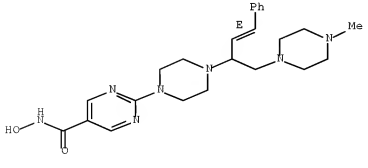
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-20-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylmethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 875139-21-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-[(4-methyl-1-piperazinyl)methyl]-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

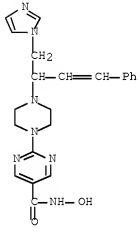
Double bond geometry as shown.



RN 875139-23-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(1H-imidazol-1-ylmethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

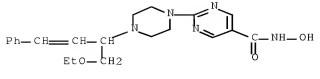
CRN 875139-22-3
CMF C22 H25 N7 O2



CM 2

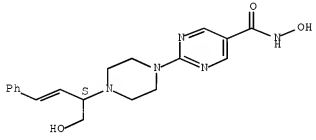
CRN 76-05-1
CMF C2 H F3 O2

RN 875139-24-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(ethoxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



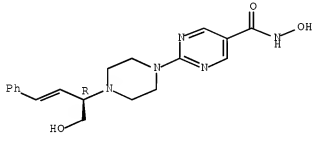
RN 875139-25-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1S)-1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



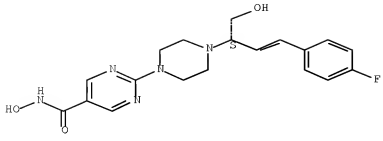
RN 875139-26-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1R)-1-(hydroxymethyl)-3-phenyl-2-propenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

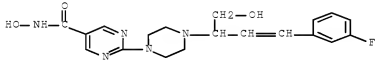


RN 875139-27-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

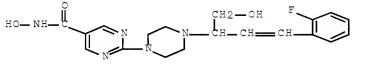
Absolute stereochemistry.
Double bond geometry unknown.



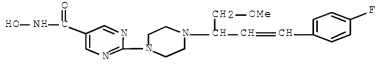
RN 875139-28-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(3-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-29-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(2-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



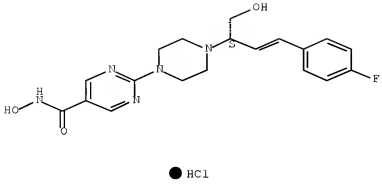
RN 875139-30-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(methoxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 875139-31-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

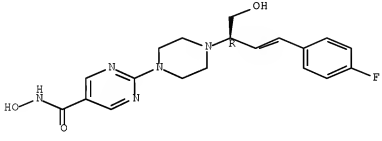
Absolute stereochemistry.

Double bond geometry unknown.



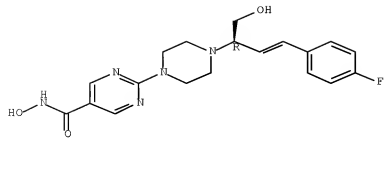
RN 875139-69-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 875139-70-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propenyl]-1-piperazinyl]-N-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

L20 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300395 CAPLUS Full-text
DOCUMENT NUMBER: 142:355054
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030705	A1	20050407	WO 2004-US31591	20040924
WO 2005030705	A9	20060420		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2539117	A1	20050407	CA 2004-2539117	20040924
EP 1663953	A1	20060607	EP 2004-789074	20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1882529	A	20061220	CN 2004-80034571	20040924
JP 2007506785	T	20070322	JP 2006-528279	20040924

PRIORITY APPLN. INFO.:

US 2003-505884P	P	20030924
US 2003-532973P	P	20031229
US 2004-561082P	P	20040409
WO 2004-US31591	W	20040924

OTHER SOURCE(S): CASREACT 142:355054; MARPAT 142:355054

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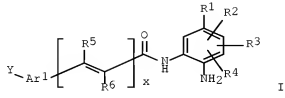

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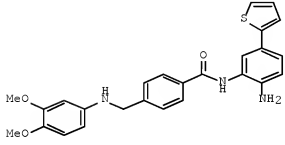


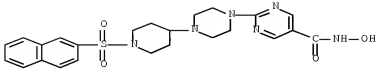
II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)- methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5- diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

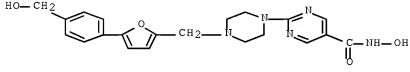
IT 603985-82-6P 603985-86-0P 603985-88-2P
603985-90-6P 603985-94-0P 603991-95-3P
603991-96-4P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-82-6 CAPLUS

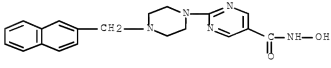
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-86-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



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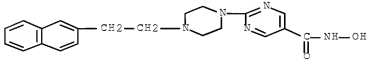
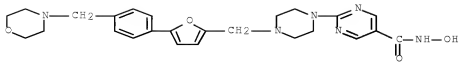
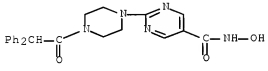


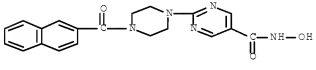
RN 603985-94-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



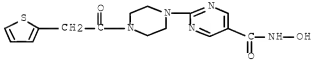
RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy-
(9CI) (CA INDEX NAME)



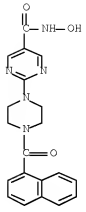
RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-
piperazinyl]- (CA INDEX NAME)



RN 603992-24-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-thienylacetyl)-1-piperazinyl]-
(9CI) (CA INDEX NAME)



RN 603992-25-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(1-naphthalenylcarbonyl)-1-
piperazinyl]- (CA INDEX NAME)



RN 603992-26-3 CAPLUS
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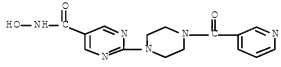
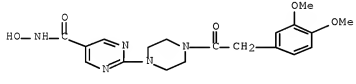


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



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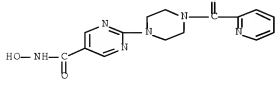
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 604784-81-8 CAPLUS
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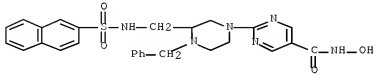

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300394 CAPLUS Full-text
DOCUMENT NUMBER: 142:373563
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030704	A1	20050407	WO 2004-US31590	20040924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 2003-505884P P 20030924
US 2003-532973P P 20031229
US 2004-561082P P 20040409

OTHER SOURCE(S): MARPAT 142:373563
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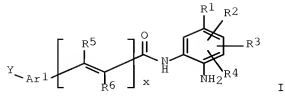

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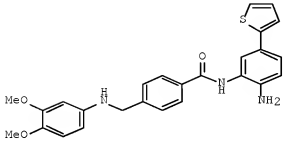


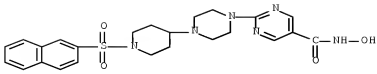
II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiophenebo ronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)- methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5- diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

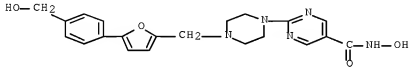
IT 603985-82-6P 603985-86-0P 603985-88-2P
603985-90-6P 603985-94-0P 603991-95-3P
603991-96-4P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-82-6 CAPLUS

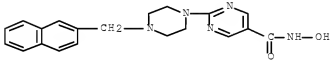
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-86-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603985-90-6 CAPLUS
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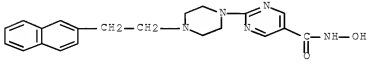
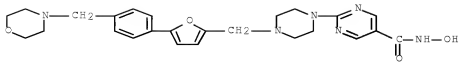
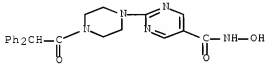


RN 603985-94-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy-
(9CI) (CA INDEX NAME)



RN 603991-96-4 CAPLUS
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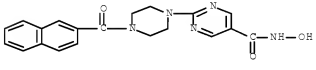

RN 603992-24-1 CAPLUS
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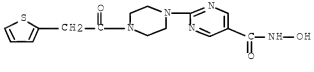

RN 603992-25-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(1-naphthalenylcarbonyl)-1-
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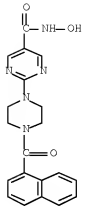
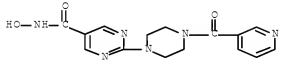
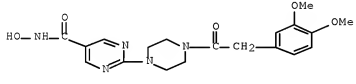


RN 603992-26-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-28-5 CAPLUS
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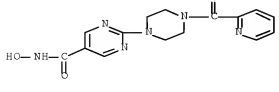

RN 604784-81-8 CAPLUS
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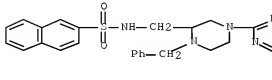

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737757 CAPLUS Full-text
DOCUMENT NUMBER: 139:276911
TITLE: Preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076438	A1	20030918	WO 2003-EP2510	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475766	A1	20030918	CA 2003-2475766	20030311
AU 2003218735	A1	20030922	AU 2003-218735	20030311
EP 1485378	A1	20041215	EP 2003-711979	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007606	A	20041221	BR 2003-7606	20030311
CN 1642948	A	20050720	CN 2003-805921	20030311
JP 2005526766	T	20050908	JP 2003-574655	20030311
NZ 534833	A	20060728	NZ 2003-534833	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02536	A	20070413	IN 2004-DN2536	20040831
US 2005165016	A1	20050728	US 2004-507084	20040908
MX 2004PA08795	A	20041126	MX 2004-PA8795	20040910
NO 2004004135	A	20040929	NO 2004-4135	20040929

PRIORITY APPLN. INFO.:

US 2002-363799P	P	20020313
WO 2002-EP14833	A	20021223
CN 2003-805921	A3	20030311
WO 2003-EP2510	W	20030311

OTHER SOURCE(S): MARPAT 139:276911

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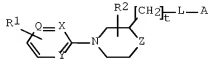

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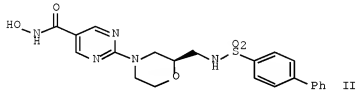


II

AB The title compds. [I; t = 0-4; Q, X, Y = N, C; Z = NH, O, CH2; R1 = CONR3R4, NHCOR7, CO(alkanediyl)SR7, etc. (wherein R3, R4 = H, OH, alkyl, etc.; R7 = H, alkyl, alkylcarbonyl, etc.); R2 = H, OH, NH2, etc.; L = NR9CO, NR9SO2, NR9CH2 (R9 = H, alkyl, cycloalkyl, etc.); A = (un)substituted Ph, cycloalkyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of (+)-II which showed pIC50 of 7.723 against HDAC, was given.

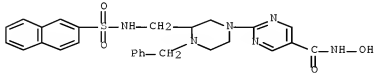
IT 604784-81-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)

RN 604784-81-8 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:737723 CAPLUS Full-text

DOCUMENT NUMBER: 139:261309

TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or diazepino)benzamides as new inhibitors of histone deacetylase

INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475764	A1	20030918	CA 2003-2475764	20030311
AU 2003218736	A1	20030922	AU 2003-218736	20030311
EP 1485353	A1	20041215	EP 2003-711980	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008081	A	20041221	BR 2003-8081	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
NZ 534834	A	20050729	NZ 2003-534834	20030311
JP 2005526067	T	20050902	JP 2003-574621	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02533	A	20070413	IN 2004-DN2533	20040831
US 2005107384	A1	20050519	US 2004-506998	20040908
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909
MX 2004PA08806	A	20041126	MX 2004-PA8806	20040910
NO 2004004194	A	20041001	NO 2004-4194	20041001

PRIORITY APPLN. INFO.:	US 2002-363799P	P	20020313
	WO 2002-EP14833	A	20021223
	CN 2003-805921	A3	20030311
	WO 2003-EP2514	W	20030311

OTHER SOURCE(S): MARPAT 139:261309

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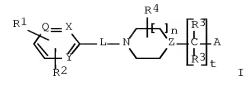

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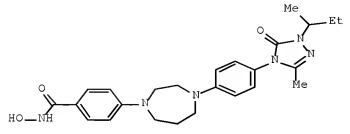


II

AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

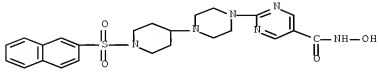
IT 603985-83-7P 603985-87-1P 603985-89-3P
603985-91-7P 603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-83-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]-, trifluoroacetate (10:9) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-82-6
CMF C24 H28 N6 O4 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-87-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

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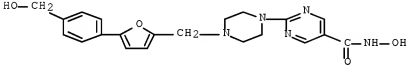
CRN 603985-86-0
CMF C21 H23 N5 O4



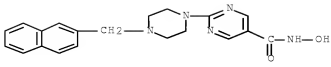
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-88-2
CMF C20 H21 N5 O2



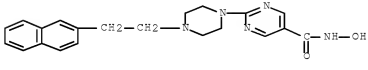
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-91-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, trifluoroacetate (5:4) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 603985-90-6
CMF C21 H23 N5 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-,

bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

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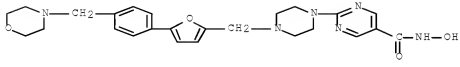
CRN 603985-94-0
CMF C25 H30 N6 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737586 CAPLUS Full-text
DOCUMENT NUMBER: 139:261308
TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases
INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

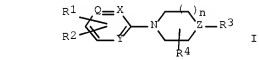
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075929	A1	20030918	WO 2003-EP2515	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2476065	A1	20030918	CA 2003-2476065		20030311
AU 2003218737	A1	20030922	AU 2003-218737		20030311
EP 1485099	A1	20041215	EP 2003-711981		20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003007624	A	20050111	BR 2003-7624		20030311
CN 1639125	A	20050713	CN 2003-805675		20030311
CN 1642551	A	20050720	CN 2003-805833		20030311
JP 2005525379	T	20050825	JP 2003-574203		20030311
NZ 534832	A	20050930	NZ 2003-534832		20030311
CN 101007803	A	20070801	CN 2007-10005212		20030311
IN 2004DN02537	A	20070112	IN 2004-DN2537		20040831
ZA 2004007237	A	20050928	ZA 2004-7237		20040909
ZA 2004007235	A	20051004	ZA 2004-7235		20040909
ZA 2004007232	A	20051006	ZA 2004-7232		20040909
ZA 2004007233	A	20051006	ZA 2004-7233		20040909
ZA 2004007234	A	20051006	ZA 2004-7234		20040909
ZA 2004007236	A	20051006	ZA 2004-7236		20040909
MX 2004PA08797	A	20041126	MX 2004-PA8797		20040910
US 2005096468	A1	20050505	US 2004-507785		20040913
NO 2004004113	A	20040928	NO 2004-4113		20040928
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			WO 2002-EP14833	A	20021223
			CN 2003-805921	A3	20030311
			WO 2003-EP2515	W	20030311

OTHER SOURCE(S): MARPAT 139:261308

GI



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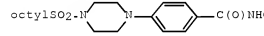


II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-

tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5- carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7 or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6- alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, C11-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1- 6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

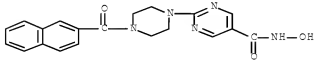
IT 603991-96-4P

RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



IT 603991-95-3P 603992-24-1P 603992-25-2P 603992-26-3P 603992-27-4P 603992-28-5P

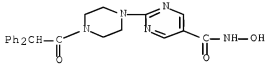
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate and reagent for detection/identification of histone

deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-(diphenylacetyl)-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-24-1 CAPLUS

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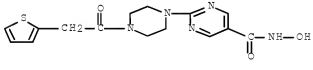

RN 603992-25-2 CAPLUS

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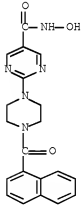

RN 603992-26-3 CAPLUS

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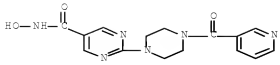
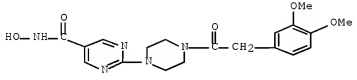


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 603992-28-5 CAPLUS
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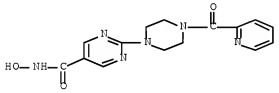

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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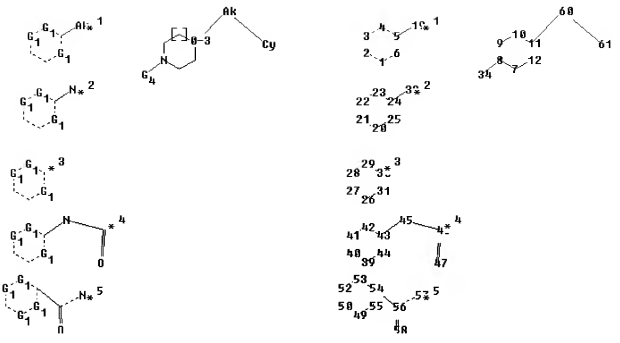

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19 32 34 45 46 47 56 57 58 60 61
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 20 21 22 23 24 25 26 27 28 29 30
31 39 40 41 42 43 44 49 50 52 53 54 55
chain bonds :
5-19 8-34 11-60 24-32 43-45 45-46 46-47 54-56 56-57 56-58 60-61
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 20-21 20-25 21-22
22-23 23-24 24-25 26-27 26-31 27-28 28-29 29-30 30-31 39-40 39-44 40-41 41-42 42-43
43-44 49-50 49-55 50-52 52-53 53-54 54-55
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-19 7-8 7-12 8-9 8-34 9-10 10-11 11-12 11-60 20-21 20-25 21-22 22-23 23-24 24-25 24-32 26-27 26-31 27-28 28-29 29-30 30-31 39-40
39-44 40-41 41-42 42-43 43-44 43-45 45-46 46-47 49-50 49-55 50-52 52-53 53-54 54-55
54-56 56-57 56-58 60-61
isolated ring systems :
containing 1 : 7 : 20 : 26 : 39 : 49 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

G4:[*1],[*2],[*3],[*4],[*5]

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Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  19:CLASS  20:Atom  21:Atom  22:Atom  23:Atom  24:Atom  25:Atom
26:Atom  27:Atom
28:Atom  29:Atom  30:Atom  31:Atom  32:CLASS  34:CLASS  39:Atom  40:Atom  41:Atom
42:Atom  43:Atom
44:Atom  45:CLASS  46:CLASS  47:CLASS  49:Atom  50:Atom  52:Atom  53:Atom  54:Atom
55:Atom  56:CLASS
57:CLASS  58:CLASS  60:CLASS  61:Atom



L21     STRUCTURE UPLOADED

=> d l21
L21 HAS NO ANSWERS
L21             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l21 full
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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



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FULL SCREEN SEARCH COMPLETED -  9832549 TO ITERATE

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  8.1% PROCESSED   799150 ITERATIONS                          3066 ANSWERS

 10.2% PROCESSED  1000000 ITERATIONS                          3732 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.48

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      9832549 TO  9832549
PROJECTED ANSWERS:           36121 TO    37269

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L23        179 L22

=> d his


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     FILE 'CAPLUS' ENTERED AT 15:42:10 ON 03 MAR 2008
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L4            466 S L3 AND INHIBIT!
L5              2 S L4 AND HISTONE DEACETYLASE

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L18             9 S L17 FULL
L19             9 S L18 FULL

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L20             9 S L19 FULL
L21               STRUCTURE UPLOADED
                  S L21

     FILE 'REGISTRY' ENTERED AT 17:29:20 ON 03 MAR 2008
L22          3732 S L21 FULL

     FILE 'CAPLUS' ENTERED AT 17:30:09 ON 03 MAR 2008
L23           179 S L22 FULL

=> s l23 full
L24           179 L22

=> s l24 and piperazine
         30370 PIPERAZINE
          3859 PIPERAZINES
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        31240 PIPERAZINE
                (PIPERAZINE OR PIPERAZINES)
L25        31 L24 AND PIPERAZINE

=> s l25 and (pyrimidine or 1,3-diazine)
        57439 PYRIMIDINE
        16127 PYRIMIDINES
        63705 PYRIMIDINE
                (PYRIMIDINE OR PYRIMIDINES)
      9521691 1
      7172173 3
         1274 DIAZINE
          711 DIAZINES
         1667 DIAZINE
                (DIAZINE OR DIAZINES)
          139 1,3-DIAZINE
                (1(W)3(W)DIAZINE)
L26         7 L25 AND (PYRIMIDINE OR 1,3-DIAZINE)

=> d ibib abs hitstr tot

L26  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:91154  CAPLUS  Full-text
DOCUMENT NUMBER:          148:191925
TITLE:                    Preparation of pyrazole derivatives as inositol
                          1,4,5-trisphosphate 3-kinase B (ITPKb) inhibitors
INVENTOR(S):              Pan, Shifeng; Liu, Yi; Xie, Yun Feng; Cheng, Dai; Wan,
                          Yongqin; Han, Dong; Yang, Yang; Gao, Wenqi; Jiang,
                          Jiqing; Bursulaya, Badry; Chamberlain, Philip;
                          Karanewsky, Donald S.; Wang, Xia
PATENT ASSIGNEE(S):       IRM LLC, Bermuda
SOURCE:                   PCT Int. Appl., 61pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2008011611        A2    20080124    WO 2007-US74048        20070720
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
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             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
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             BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       US 2006-832681P     P  20060721
                                             US 2007-893874P     P  20070308
GI
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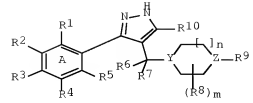

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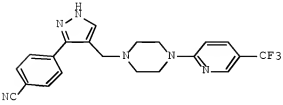


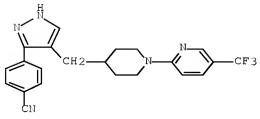
II

AB 3-Aryl- or 3-heteroaryl-1H-pyrazole derivs. [I; n = 0-3; m = 0-3; A can have up to 3 groups selected from -CR1=, -CR2=, -CR3=, -CR4= and -CR5= replaced with N; R1-R5 independently H, HO, halo, cyano, C1-6 alkyl, halo-C1-6 alkyl, hydroxy-C1-6 alkyl, cyano-C1-6 alkyl, C3-8 heterocycloalkyl-C0-4 alkyl, C1-10 heteroaryl-C0-4 alkyl, -XSO2R11, -XSO2NR11R12, -XSO2NR11C(O)R12, -XC(NR11)NR11OR12, -XCR11=NOR12, -XC(O)R11, -XC(O)OR11, etc.; X = independently a bond or C1-4 alkylene; R11 = H, C1-6 alkyl; R12 = H, C1-6 alkyl, C6-10 aryl; or NR11R12 together forms a C3-8 heterocycloalkyl; R6, R7 = independently H or C1-3 alkyl; or CR6R7 together forms C3-7 cycloalkyl; R8 = C1-6 alkyl, halo-C1-3 alkyl, C1-6 alkoxy, -CH2OR8a, -CO2R8a, C2-6 alkenyl; or two R8 groups attached to different carbon atoms can combine to form an alkyl bridge; or two R8 groups attached to the same carbon can form a C3-8 cycloalkyl or carbonyl group; R8a = H, C1-6 alkyl; R9 = each (un)substituted C6-10 aryl or C1-10 heteroaryl; R10 = H, C1-6 alkyl, -NR15R16, -NR15C(O)R16, -C(O)NR15R16; R15, R16 = independently H, C1-6 alkyl, or each (un)substituted C6-10 aryl, C1-10 heteroaryl, C3-12 cycloalkyl, or C3-8 heterocycloalkyl; Y, Z = independently CR20 or N; R20 = H or C1-4 alkyl] and pharmaceutically acceptable salts thereof are prepared These compds. are useful to treat or prevent diseases or disorders associated with abnormal or deregulated B cell activities, particularly diseases or disorders that involve aberrant activation of inositol 1,4,5-trisphosphate 3-kinase B (ITPKb), e.g. autoimmune diseases, rheumatoid arthritis, and systemic lupus erythematosus, and B cell lymphoma. Thus, a solution of 60 mg 4-(4-formyl-1H-3-yl)benzonitrile, 34.7 mg 1-[5-(trifluoromethyl)pyrid-2- yl]piperazine, and 25 μL glacial acetic acid in 5 mL methanol was stirred at room temperature for 30 min followed by the addition of 127 mg sodium triacetoxyborohydride in a single portion. The resulting mixture was heated at 40° for 1 h, and then cooled to room temperature to give, after HPLC purification and neutralization of the trifluoroacetate salt, 4-[4-[4-(5-trifluoromethylpyridin-2-yl)piperazin-1-ylmethyl]-1H-pyrazol-3- yl]benzonitrile (II) as a white solid.

IT 1003019-12-2P, 4-[4-[[1-[5-(Trifluoromethyl)pyridin-2-yl]piperidin-4-yl]methyl]-1H-pyrazol-3-yl]benzonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazole derivs. as inositol 1,4,5-trisphosphate 3-kinase B (ITPKb) inhibitors for prevention and/or treatment autoimmune diseases, rheumatoid arthritis, and systemic lupus erythematosus, and B cell lymphoma)

RN 1003019-12-2 CAPLUS

CN Benzonitrile, 4-[4-[[1-[5-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]methyl]-1H-pyrazol-3-yl]- (CA INDEX NAME)



L26 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:43697 CAPLUS Full-text
DOCUMENT NUMBER: 148:121730
TITLE: Preparation of pyrimidines and related compounds for the treatment of cell proliferative diseases
INVENTOR(S): Engelhardt, Harald; Bader, Gerd; Boehmelt, Guido; Brueckner, Ralph; Gerstberger, Thomas; Impagnatiello, Maria; Kuhn, Daniel; Schaaf, Otmar; Stadtmueller, Heinz; Waizenegger, Irene; Zoephel, Andreas
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: PCT Int. Appl., 67pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008003766	A2	20080110	WO 2007-EP56853	20070705
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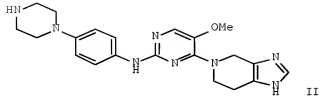
PRIORITY APPLN. INFO.: EP 2006-116748 A 20060706
OTHER SOURCE(S): MARPAT 148:121730
GI

I



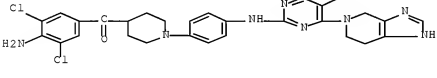
II

AB Title compds. I [X = CH or N; R1 = heterocycloalkyl (optionally substituted with alkyl, cycloalkyl, aryl, etc.); R2 = aryl, heterocycloalkyl or heteroaryl; R3 = halo, -CN, alkyl, etc.] or tautomers, racemates, enantiomers, diastereomers, or mixts. thereof, or pharmacol. acceptable acid salts thereof were prepared Thus, a multi-step synthesis of compound II, starting from 1-(benzyloxycarbonyl)piperazine, was given. Compds. I herein were tested for PDK1 kinase inhibition and antiproliferative activity. Pharmaceutical composition comprising compds. I is disclosed.

IT 1001000-50-5P 1001000-51-6P 1001003-24-2P
1001003-25-3P 1001003-26-4P 1001003-27-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidines and related compds. for treatment of diseases characterized by excessive or abnormal cell proliferation)

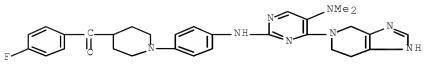
RN 1001000-50-5 CAPLUS

CN Methanone, (4-amino-3,5-dichlorophenyl)[1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl]- (CA INDEX NAME)

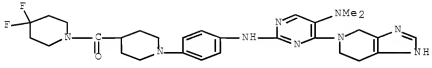


RN 1001000-51-6 CAPLUS

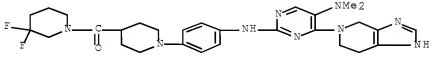
CN Methanone, [1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl](4-fluorophenyl)- (CA INDEX NAME)



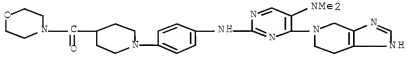
RN 1001003-24-2 CAPLUS
CN Methanone, (4,4-difluoro-1-piperidinyl)[1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl]- (CA INDEX NAME)



RN 1001003-25-3 CAPLUS
CN Methanone, (3,3-difluoro-1-piperidinyl)[1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl]- (CA INDEX NAME)

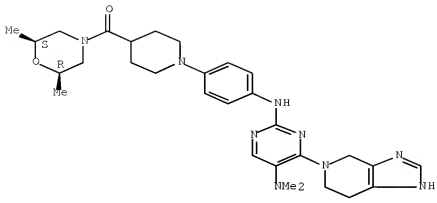


RN 1001003-26-4 CAPLUS
CN Methanone, [1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl]-4-morpholinyl- (CA INDEX NAME)



RN 1001003-27-5 CAPLUS
CN Methanone, [1-[4-[[5-(dimethylamino)-4-(3,4,6,7-tetrahydro-5H-imidazo[4,5-c]pyridin-5-yl)-2-pyrimidinyl]amino]phenyl]-4-piperidinyl][(2R,6S)-2,6-dimethyl-4-morpholinyl]-, rel- (CA INDEX NAME)

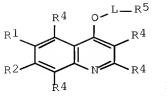
Relative stereochemistry.



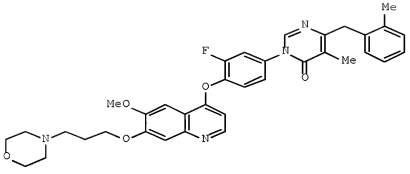
L26 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1454807 CAPLUS Full-text
DOCUMENT NUMBER: 148:78895
TITLE: Preparation of quinoline derivatives as tyrosine kinases inhibitors
INVENTOR(S): Gaudino, John; Boyd, Steven Armen; Marlow, Allison L.; Kaplan, Tomas; Fong, Kin Chiu; Seo, Jeongbeob; Tian, Honggi; Blake, James; Koch, Kevin
PATENT ASSIGNEE(S): Array Biopharma Inc., USA; Genentech, Inc.
SOURCE: PCT Int. Appl., 189pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007146824	A2	20071221	WO 2007-US70787	20070608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2006-811909P P 20060608
OTHER SOURCE(S): MARPAT 148:78895
GI



I



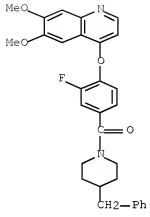
II

AB Title compds. represented by the formula I [wherein R1, R2, R4 = independently H, halo, CN, etc.; with the proviso that at least one of R1 and R2 is not H; L = (un)substituted (hetero)cyclyl or (hetero)aryl; R5 = -COH, (un)substituted amino, heterocyclyl, etc.; and stereoisomers, geometric isomers, tautomers, solvates, metabolites, and salts thereof] were prepared as tyrosine kinases inhibitors. For example, II was provided in a multi-step synthesis starting from the reaction of (2-methylbenzyl)zinc chloride with 4,6-dichloro-5-methylpyrimidine. Certain compds. of this invention had MKN45 cell-based activity IC50 values less than 100 nM. Thus, I and their pharmaceutical compns. are useful for inhibiting receptor tyrosine kinases and for treating hyperproliferative disorders mediated thereby.

IT 960297-78-3P, (4-Benzylpiperidin-1-yl)[4-[(6,7-dimethoxyquinolin-4-yl)oxy]-3-fluorophenyl]methanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline derivs. as tyrosine kinases inhibitors)

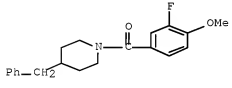
RN 960297-78-3 CAPLUS

CN Methanone, [4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl][4-(phenylmethyl)-1-piperidinyl]- (CA INDEX NAME)

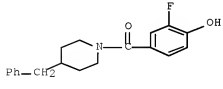


IT 960297-79-4P, (4-Benzylpiperidin-1-yl)(3-fluoro-4-methoxyphenyl)methanone 960297-80-7P, (4-Benzylpiperidin-1-yl)(3-fluoro-4-hydroxyphenyl)methanone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline derivs. as tyrosine kinases inhibitors)

RN 960297-79-4 CAPLUS
CN Methanone, (3-fluoro-4-methoxyphenyl)[4-(phenylmethyl)-1-piperidinyl]- (CA INDEX NAME)



RN 960297-80-7 CAPLUS
CN Methanone, (3-fluoro-4-hydroxyphenyl)[4-(phenylmethyl)-1-piperidinyl]- (CA INDEX NAME)



L26 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1392131 CAPLUS Full-text
DOCUMENT NUMBER: 148:55104

TITLE: Pyrrolo[1,2-a]pyrazin-1(2H)-one and pyrrolo[1,2-d][1,2,4]triazin-1(2H)-one derivatives as inhibitors of poly(ADP-ribose)polymerase (PARP) and their preparation, pharmaceutical compositions and use in the treatment of diseases

INVENTOR(S): Jones, Philip; Kinzel, Olaf; Llauger Bufi, Laura; Muraglia, Ester; Pescatore, Giovanna; Torrisi, Caterina

PATENT ASSIGNEE(S): Istituto di Ricerche di Biologia Molecolare P. Angeletti SpA, Italy

SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007138355	A1	20071206	WO 2007-GB50300	20070529

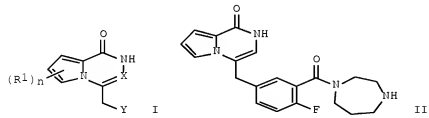
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2006-10670 A 20060531
GB 2007-7359 A 20070417

OTHER SOURCE(S): MARPAT 148:55104

GI

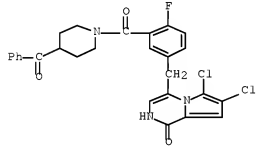


AB The invention relates to compds. of formula I: and pharmaceutically acceptable salts or tautomers thereof which are inhibitors of poly(ADP-ribose)polymerase (PARP) and thus useful for the treatment of cancer, inflammatory diseases, reperfusion injuries, ischemic conditions, stroke, renal failure, cardiovascular diseases, vascular diseases other than cardiovascular diseases, diabetes mellitus, neurodegenerative diseases, retroviral infections, retinal

damage, skin senescence and UV-induced skin damage, and as chemo- or radiosensitizers for cancer treatment. Compds. of formula I wherein n is 0, 1, 2, and 3; X is N and CH; Y is (un)substituted Ph and (un)substituted 5-membered unsatd. heterocycle; and their pharmaceutically acceptable salts and tautomers thereof, are claimed. Example compound II•TFA was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their PARP inhibitory activity.

IT 959768-13-9P, 4-[3-[(4-Benzoylpiperidin-1-yl)carbonyl]-4-fluorobenzyl]-6,7-dichloropyrrolo[1,2-a]pyrazin-1(2H)-one 959768-56-0P 959768-59-3P, 1-[[1-[5-[(6,7-Dichloro-1-oxo-1,2-dihydropyrrolo[1,2-a]pyrazin-4-yl)methyl]-2-fluorobenzoyl]piperidin-4-yl]methyl]-1H-imidazole trifluoroacetate 959770-22-0P, 1-[1-[5-[(6,7-Dichloro-1-oxo-1,2-dihydropyrrolo[1,2-a]pyrazin-4-yl)methyl]-2-fluorobenzoyl]piperidin-4-yl]-4-methylpiperidine trifluoroacetate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrrolopyrazinone and pyrrolotriazinone derivs. as poly(ADP-ribose)polymerase inhibitors useful in the treatment of diseases)

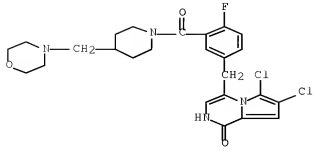
RN 959768-13-9 CAPLUS
CN Pyrrolo[1,2-a]pyrazin-1(2H)-one, 4-[[3-[(4-benzoyl-1-piperidinyl)carbonyl]-4-fluorophenyl]methyl]-6,7-dichloro- (CA INDEX NAME)



RN 959768-56-0 CAPLUS
CN Pyrrolo[1,2-a]pyrazin-1(2H)-one, 6,7-dichloro-4-[[4-fluoro-3-[[4-(4-morpholinylmethyl)-1-piperidinyl]carbonyl]phenyl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 959768-55-9
CMF C25 H27 C12 F N4 O3



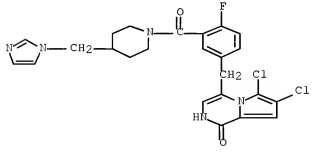
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 959768-59-3 CAPLUS
CN Pyrrolo[1,2-a]pyrazin-1(2H)-one, 6,7-dichloro-4-[[4-fluoro-3-[[4-(1H-imidazol-1-ylmethyl)-1-piperidinyl]carbonyl]phenyl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 959768-58-2
CMF C24 H22 Cl2 F N5 O2



CM 2

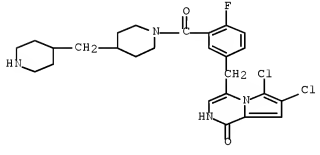
CRN 76-05-1

CMF C2 H F3 O2

RN 959770-22-0 CAPLUS
CN Pyrrolo[1,2-a]pyrazin-1(2H)-one, 6,7-dichloro-4-[[4-fluoro-3-[[4-(4-piperidinylmethyl)-1-piperidinyl]carbonyl]phenyl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 959770-21-9
CMF C26 H29 Cl2 F N4 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:108827 CAPLUS Full-text
DOCUMENT NUMBER: 147:385848
TITLE: Trifluoroacetyl-substituted heterocycles as histone deacetylase inhibitors, their preparation,

pharmaceutical compositions, and use in therapy

INVENTOR(S): Jones, Philip; Ontoria Ontoria, Jesus Maria; Schultz-Fademrecht, Carsten

PATENT ASSIGNEE(S): Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A., Italy

SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007107594	A2	20070927	WO 2007-EP52712	20070321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2006-5573 A 20060321

OTHER SOURCE(S): MARPAT 147:385848

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to trifluoroacetyl-substituted heterocycles of formula I, which are inhibitors of histone deacetylase (HDAC), particularly class II HDAC. In compds. I, each of X, Y, and Z is independently selected from N and CH; and each of R1 and R2 is independently selected from H, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, C6-10 aryl, C6-10 aryl-C1-6 alkyl, C6-10 aryl-C1-6 alkoxy, 5- to 10-membered heterocyclyl, and 5- to 10-membered heteroaryl, or R1 and R2, together with the nitrogen atom to which they are attached, form (un)substituted 4- to 7-membered heterocyclyl; including salts and tautomers thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of conditions that respond to histone deacetylase inhibition, such as cellular proliferative diseases, neurodegenerative diseases, schizophrenia, and stroke. Addition of (trifluoromethyl)trimethylsilane to 6-fluoro-3-pyridinecarboxaldehyde followed by oxidation formed ketone II, which underwent substitution with 4-phenylpiperidin-4-ol to give the trifluoroacetate salt of (trifluoroacetyl)pyridine III. The compds. of the invention, e.g., III, expressed IC50 values of less than 10 μM in the assays used (no specific data).

IT 950697-64-6P, 2-(3-Benzylpyrrolidin-1-yl)-5-(trifluoroacetyl)pyridine trifluoroacetate 950697-68-0P, 2-(4-Benzoylpiperidin-1-yl)-5-(trifluoroacetyl)pyridine trifluoroacetate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

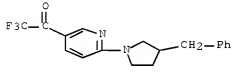
(Uses)
(drug candidate; preparation of trifluoroacetyl-substituted heterocycles as histone deacetylase inhibitors)

RN 950687-64-6 CAPLUS

CN Ethanone, 2,2,2-trifluoro-1-[6-[3-(phenylmethyl)-1-pyrrolidinyl]-3-pyridinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 950687-63-5
CMF C18 H17 F3 N2 O



CM 2

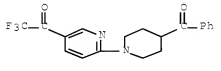
CRN 76-05-1
CMF C2 H F3 O2

RN 950687-68-0 CAPLUS

CN Ethanone, 1-[6-(4-benzoyl-1-piperidinyl)-3-pyridinyl]-2,2,2-trifluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 950687-67-9
CMF C19 H17 F3 N2 O2



CM 2

CRN 76-05-1

CMF C2 H F3 O2

L26 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:672604 CAPLUS Full-text
DOCUMENT NUMBER: 147:95662
TITLE: Polycyclic indazole derivatives that are ERK inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Cooper, Alan; Deng, Yongqi; Shipps, Gerald W., Jr.; Shih, Neng-Yang; Zhu, Hugh; Sun, Robert; Kelly, Joseph; Doll, Ronald; Nan, Yang; Wang, Tong; Desai, Jagdish; Wang, James; Dong, Youhao; Madison, Vincent S.; Li, Xiao; Hruza, Alan; Siddiqui, M. Arshad; Samatar, Ahmed; Paliwal, Sunil; Tsui, Hon-Chung; Celebi, Azim A.; Wu, Yiji; Boga, Sobhana Babu
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 505pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007070398	A1	20070621	WO 2006-US46959	20061211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007191604	A1	20070816	US 2006-636954	20061211
PRIORITY APPLN. INFO.:			US 2005-749856P P	20051213
OTHER SOURCE(S):	MARPAT 147:95662			

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are the ERK inhibitors of formula I and the pharmaceutically acceptable salts and solvates thereof. Compds. of formula I wherein Q is

(un)substituted piperidine or piperazine ring that can have a bridge or a fused ring; Y1, Y2, and Y3 are independently CH=, N=, etc.; n is 1 to 3; R1 is CN, NO2, OH and derivs., SH and derivs., acyl, etc.; R2 is H, CN, halo, (un)substituted alkyl, alkynyl, alkenyl, etc.; R8 is H, OH, NH2 and derivs., alkyl, and aminocarbonyl; each R35 is independently H and C1-6 alkyl; R36 is H, alkyl, and alkoxy; and their pharmaceutically acceptable salts thereof, are claimed. Also disclosed are methods of treating cancer using the compds. of formula I. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their ERK inhibitory activity (data given).

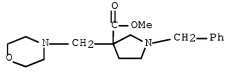
IT 942190-26-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of polycyclic indazole derivs. as ERK inhibitors and their use in the treatment and prevention of cancer)

RN 942190-26-3 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 3-(4-morpholinylmethyl)-1-(phenylmethyl)-, methyl ester (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:619346 CAPLUS Full-text

DOCUMENT NUMBER: 147:52936

TITLE: Preparation of alicyclic heterocycles as CCR4 function regulators

INVENTOR(S): Furukubo, Shigeru; Miyazaki, Hiroshi

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan

SOURCE: PCT Int. Appl., 184pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007063934	A1	20070607	WO 2006-JP323908	20061130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-348597 A 20051202
US 2005-750038P P 20051214

OTHER SOURCE(S): MARPAT 147:52936

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [ring A = Q1, etc.; ring B = (un)substituted aromatic hydrocarbon ring, (un)substituted heterocycle; P1, P2 = CH, N with the proviso that P1 and P2 can not be CH simultaneously; q, r = 0-2; m = 1, 2; X = -N(R7)-, -O-, -C(R8)(R9)-; Y = -C(R10)(R11)-, -CO-, -SO2-; Z = alkylene (optionally substituted with oxo), -CON(R12)-, -SO2N(R12)-, etc.; R1 = H, alkyl, alkoxy, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; R3 = (un)substituted hydrocarbon ring, (un)substituted heterocycle, hydroxy, etc.; R7 = H, alkyl; R8, R9, R10, and R11 = H, alkyl; R12 = H, alkyl] and their pharmaceutically acceptable salts were prepared For example, reaction of (5-chloro-pyrazolo[1,5-a]pyrimidin-7-yl)-(2,4-dichloro-benzyl)amine, e.g, prepared from 3-aminopyrazole in 3 steps, with (R)-2-(piperazine-1-carbonyl)-pyrrolidine-1-carboxylic acid tert-Bu ester followed by treatment with trifluoroacetic acid afforded compound II. Of note, compds. I are useful as CCR4 function regulators for the treatment of bronchial asthma and atopic dermatitis (no data).

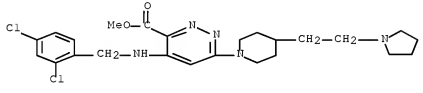
IT 939977-40-9P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of alicyclic heterocycles as CCR4 function regulators)

RN 939977-40-9 CAPLUS

CN 3-Pyridazinecarboxylic acid, 4-[[(2,4-dichlorophenyl)methyl]amino]-6-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]-, methyl ester (CA INDEX NAME)



IT 939976-73-5P 939977-36-3P 939977-38-5P
939977-50-1P 939977-60-3P 939977-85-2P
939977-87-4P 939978-11-7P 939978-12-8P
939978-17-3P 939978-18-4P 939978-19-5P
939978-26-4P 939978-34-4P 939978-35-5P
939978-36-6P

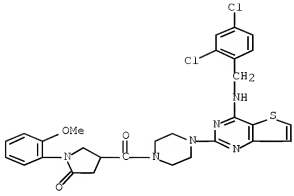
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of alicyclic heterocycles as CCR4 function regulators)

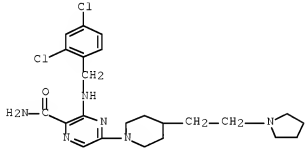
RN 939976-73-5 CAPLUS

CN 2-Pyrrolidinone, 4-[[4-[4-[[(2,4-dichlorophenyl)methyl]amino]thieno[3,2-d]pyrimidin-2-yl]-1-piperazinyl]carbonyl]-1-(2-methoxyphenyl)- (CA INDEX

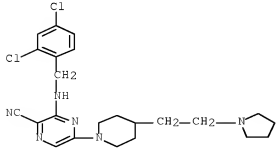
NAME)



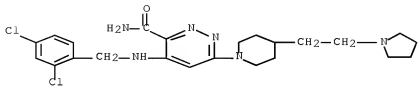
RN 939977-36-3 CAPLUS
CN 2-Pyrazinecarboxamide, 3-[[(2,4-dichlorophenyl)methyl]amino]-5-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



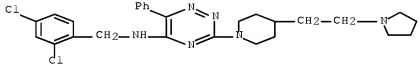
RN 939977-38-5 CAPLUS
CN 2-Pyrazinecarbonitrile, 3-[[(2,4-dichlorophenyl)methyl]amino]-5-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



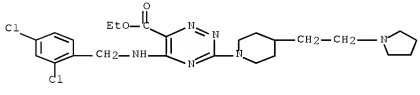
RN 939977-50-1 CAPLUS
CN 3-Pyridazinecarboxamide, 4-[[(2,4-dichlorophenyl)methyl]amino]-6-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



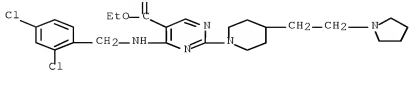
RN 939977-60-3 CAPLUS
CN 1,2,4-Triazin-5-amine, N-[(2,4-dichlorophenyl)methyl]-6-phenyl-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



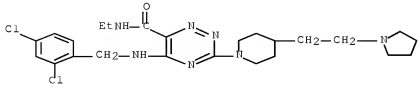
RN 939977-85-2 CAPLUS
CN 1,2,4-Triazine-6-carboxylic acid, 5-[[(2,4-dichlorophenyl)methyl]amino]-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]-, ethyl ester (CA INDEX NAME)



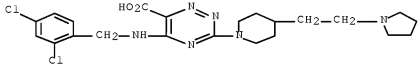
RN 939977-87-4 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 4-[[(2,4-dichlorophenyl)methyl]amino]-2-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]-, ethyl ester (CA INDEX NAME)



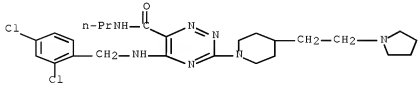
RN 939978-11-7 CAPLUS
CN 1,2,4-Triazine-6-carboxamide, 5-[[(2,4-dichlorophenyl)methyl]amino]-N-ethyl-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



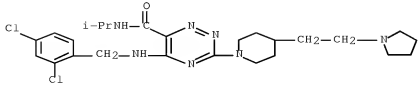
RN 939978-12-8 CAPLUS
CN 1,2,4-Triazine-6-carboxylic acid, 5-[[(2,4-dichlorophenyl)methyl]amino]-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



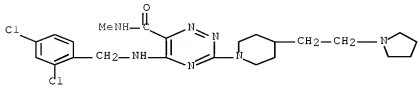
RN 939978-17-3 CAPLUS
CN 1,2,4-Triazine-6-carboxamide, 5-[[(2,4-dichlorophenyl)methyl]amino]-N-propyl-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



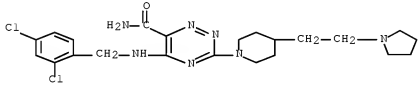
RN 939978-18-4 CAPLUS
CN 1,2,4-Triazine-6-carboxamide, 5-[[(2,4-dichlorophenyl)methyl]amino]-N-(1-methylethyl)-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



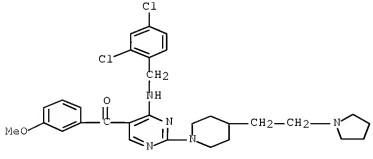
RN 939978-19-5 CAPLUS
CN 1,2,4-Triazine-6-carboxamide, 5-[[(2,4-dichlorophenyl)methyl]amino]-N-methyl-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



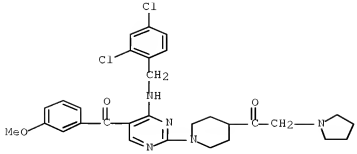
RN 939978-26-4 CAPLUS
CN 1,2,4-Triazine-6-carboxamide, 5-[[(2,4-dichlorophenyl)methyl]amino]-3-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



RN 939978-34-4 CAPLUS
CN Methanone, [4-[[(2,4-dichlorophenyl)methyl]amino]-2-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]-5-pyrimidinyl](3-methoxyphenyl)- (CA INDEX NAME)

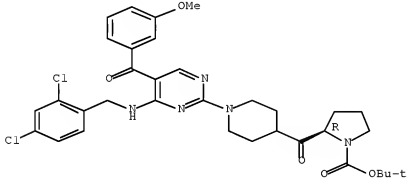


RN 939978-35-5 CAPLUS
CN Ethanone, 1-[1-[4-[[(2,4-dichlorophenyl)methyl]amino]-5-(3-methoxybenzoyl)-2-pyrimidinyl]-4-piperidinyl]-2-(1-pyrrolidinyl)- (CA INDEX NAME)

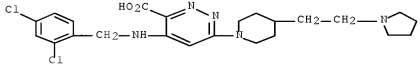


RN 939978-36-6 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[1-[4-[[(2,4-dichlorophenyl)methyl]amino]-5-(3-methoxybenzoyl)-2-pyrimidinyl]-4-piperidinyl]carbonyl]-, 1,1-dimethylethyl ester, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 939979-21-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alicyclic heterocycles as CCR4 function regulators)
RN 939979-21-2 CAPLUS
CN 3-Pyridazinecarboxylic acid, 4-[[(2,4-dichlorophenyl)methyl]amino]-6-[4-[2-(1-pyrrolidinyl)ethyl]-1-piperidinyl]- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'CAPLUS' ENTERED AT 15:42:10 ON 03 MAR 2008
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L4            466 S L3 AND INHIBIT!
L5              2 S L4 AND HISTONE DEACETYLASE

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L8              9 S L7 FULL

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L16            11 S L15

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                  S L15

     FILE 'REGISTRY' ENTERED AT 17:25:53 ON 03 MAR 2008
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L19             9 S L18 FULL

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                  S L21

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L24           179 S L23 FULL
L25            31 S L24 AND PIPERAZINE
L26             7 S L25 AND (PYRIMIDINE OR 1,3-DIAZINE)
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=> log y
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